ABSTRACT

TITLE OF THE ABSTRACT : Study of the relationship between initial autonomic functions and subsequent motor and sensory recovery, in traumatic cervical spinal cord injury patients.

DEPARTMENT	:	Physiology
NAME OF THE CANDIDATE	:	Dr. N. Latha
DEGREE AND SUBJECT	:	MD Physiology
NAME OF THE GUIDE	:	Dr. Elizabeth Tharion

OBJECTIVES:

To study whether autonomic pathway integrity assessed through the sympathetic skin response and short-term heart rate variability indices, is useful for prognostication in traumatic cervical spinal cord injury quadriplegic patients.

METHODS:

Short-term heart rate variability (HRV) indices computed in 24 cervical spinal cord injuryAIS grade A/B patients, at the time of admission, were correlated with the change in motor and sensory scores at the end of the rehabilitation programme, using Spearman's correlation coefficient. Fisher's exact test was used to study the association between the presence/absence of sympathetic skin response (SSR) at the time of admission and the change in AIS grade at the end of the rehabilitation programme.

RESULTS:

There was no statistically significant correlation between the HRV indices and the change in motor and sensory scores. Neither was there any statistically significantassociation between the presence or absence of SSR at the time of admission and the subsequent improvement in AIS grade. The findings of the present study indicate that HRV indices and SSR are not useful parameters to prognosticate recovery in traumatic cervical spinal cord injury quadriplegic patients.

KEY WORDS:

Spinal cord injury, ASIA Impairment scale, Autonomic nervous system, Heart rate variability, Short-term heart rate variability indices, Sympathetic skin response.

STUDY OF THE RELATIONSHIP BETWEEN INITIAL AUTONOMIC FUNCTIONS AND SUBSEQUENT MOTOR AND SENSORY RECOVERY, IN TRAUMATIC CERVICAL SPINAL CORD INJURY PATIENTS

A Dissertation submitted in partial fulfillment of the requirement for the

Degree of Doctor of Medicine in Physiology (Branch – V)

Of The Tamilnadu Dr. M.G.R Medical University,

Chennai -600 032

By

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CERTIFICATE

This is to certify that the thesis entitled "**Study of the relationship between initial autonomic functions and subsequent motor and sensory recovery, in traumatic cervical spinal cord injury patients**" is a bonafide, original work carried out by Dr. N. Latha, in partial fulfillment of the rules and regulations for the M.D – Branch V Physiology examination of the Tamilnadu Dr. M.G.R. Medical University, Chennai to be held in April - 2014.

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DECLARATION

I hereby declare that the investigations that form the subject matter for the thesis entitled "**Study of the relationship between initial autonomic functions and subsequent motor and sensory recovery, in traumatic cervical spinal cord injury patients**" were carried out by me during my term as a post graduate student in the Department of Physiology, Christian Medical College, Vellore. This thesis has not been submitted in part or full to any other university.

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INTRODUCTION Spinal cord injury (SCI) results in multisystem dysfunction. It is a devastating event which often leads to permanent neurological deficits. Recovery of the SCI quadriplegic patient depends to a large extent on the amount of tract fibres that are intact. Currently the SCI patients are classified based on the extent of preserved motor and sensory functions into American Spinal Injury Association (ASIA) Impairment Scale (AIS) grade A,B,C,D and E (in the order of least to most preserved motor and sensory functions (AIS 2013) This classification does not take into account the intactness of the autonomic fibres. Some of the patients show functional improvement by the end of the...

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To study whether autonomic pathway integrity assessed through the sympathetic skin response and short-term heart rate variability indices, is useful for prognostication in traumatic cervical spinal cord injury quadriplegic patients.

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Short-term heart rate variability (HRV) indices computed in 24 cervical spinal cord injury AIS grade A/B patients, at the time of admission, were correlated with the change in motor and sensory scores at the end of the rehabilitation programme, using Spearman's correlation coefficient. Fisher's exact test was used to study the association between the presence/absence of sympathetic skin response (SSR) at the time of admission and the change in AIS grade at the end of the rehabilitation programme.

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There was no statistically significant correlation between the HRV indices and the change in motor and sensory scores. Neither was there any statistically significant association between the presence or absence of SSR at the time of admission and the subsequent improvement in AIS grade. The findings of the present study indicate that HRV indices and SSR are not useful parameters to prognosticate recovery in traumatic cervical spinal cord injury quadriplegic patients.

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This classification does not take into account the intactness of the autonomic fibres. Some of the patients show functional improvement by the end of the rehabilitation programme and shift to higher AIS grades. As of now it is not possible to predict accurately which patients will improve. When a cervical SCI patient is admitted for rehabilitation, the clinicians are faced with the dilemma of predicting the recovery in them. The patients themselves and their relatives would like to know the extent to which the patient will recover functionally after rehabilitation.

In a quadriplegic patient with a complete lesion of the spinal cord above T1 spinal segmental level, the parasympathetic vagal supply to the heart will be intact, while the cardiac sympathetic supply, which originates from T1-T4 spinal segments, will lose its control from the higher brain centres. Similarly the thoraco-lumbar spinal sympathetic centres which supply the visceral organs, vascular smooth muscles and the sweat glands lose their higher control from the brain. Thus in a complete spinal cord lesion above T1 spinal segment, there will be disruption of the higher autonomic control of both the cardiac sympathetic supply and the sudomotor sympathetic supply to the sweat glands. This fact can be put to use to evaluate the integrity of the

descending autonomic pathways by testing the functioning of the cardiac autonomic activity and the sweat gland activity. When the descending autonomic pathways are completely cut as in a complete spinal cord lesion, there will be impairment of cardiac autonomic activity as measured by Heart rate variability (HRV) analysis and impairment of sweat gland function as measured by the Sympathetic skin response (SSR).

The absence of the higher centre stimuli driving the cardiac sympathetic supply alters the cardiac sympathetic drive to the SA node. This will result in altered Heart rate variability (HRV) indices, as has been previously reported in spinal cord injury patients with established complete lesion.(Claydon & Krassioukov 2008)(Grimm et al. 1997) However, if the lesion is incomplete, there may be sparing of the autonomic fibres which may reflect in the HRV indices. Currently, the SCI patients are assessed based only on the motor and sensory functions. However there is a felt need for including information about the autonomic functions of these patients also during the initial evaluation of these patients, especially when grading them functionally. The traumatic SCI patients show improvement in the motor and sensory scores and a shift from lower AIS grades (A and B) to higher grades (C, D and E).We postulate that if the HRV indices are computed at the time of admission it will provide information about whether the sympathetic control of the heart is intact or not. This information will add to the material available for prognostication.

The sympathetic skin response (SSR) involves recording a potential difference (voltage change in millivolts) from the surface of the skin, attributable to sudomotor activity.(Shahani et al. 1984) It is a simple, noninvasive electrophysiological test to investigate the integrity of the sympathetic nervous system pathways. The SSR is an intersegmental, multisynaptic, somato-sympathetic reflex such that localized cutaneous stimulation or other arousal stimuli

may elicit a diffuse intersegmental response via sympathetic nerves. SSR can be used to study the central sympathetic pathway in spinal cord injury.(Cariga et al. 2002) The SSR may be elicited either directly or reflexly. The direct response is obtained by stimulating a peripheral nerve, while the reflex response is obtained by other modes of stimulation such as a startling sound, deep inspiratory gasp or visual stimuli.(Nagarajarao et al. 2006) The SSR has been used in spinal cord injury patients to assess the state of the sympathetic system.(Curt et al. 1996)(Ogura et al. 2004)

In quadriplegic patients with complete lesion above T1, the higher centre control of the sudomotor fibres will be lost, hence increase in sudomotor activity in response to a startling stimuli such as a loud noise, visual stimuli, deep inspiratory gasp or painful electrical stimulation of the supra-orbital nerve will be absent. This will reflect in an absent SSR in response to these stimuli which activate the central fibres. On the other hand, if the descending autonomic fibres controlling the spinal sudomotor neurons are intact, the SSR to above stimuli will be present. Thus it may be possible to identify the quadriplegic patients who may show good motor and sensory recovery, by assessing the integrity of the autonomic tract fibres through SSR, at the time of admission. This will also aid in prognostication.

There are no studies relating cardiac autonomic control and intactness of the autonomic fibres, with motor and sensory recovery in SCI patients. Therefore, there is a need for studying the autonomic functions in relation with recovery in SCI patients. This study will be useful in understanding the relationship between integrity of the descending autonomic control of spinal sympathetic centres as assessed at the time of admission through HRV and SSR and subsequent motor and sensory recovery, in traumatic cervical SCI patients.

The hypothesis for this study was that those patients with higher HRV indices would have intact descending autonomic fibres and therefore the chance for some motor and sensory fibres also being intact in them and hence greater recovery would be expected in them. On the other hand those patients with lower HRV indices would have complete lesion of both the autonomic fibres as well as the motor and sensory fibres and hence poorer recovery would be expected in them. Similarly, it was hypothesized that those patients with positive SSR would have intact descending autonomic pathway and hence the chance for some intact motor and sensory fibres and therefore, greater recovery would be expected in them. While those patients with negative SSR would have complete lesion of both the autonomic fibres and the motor and sensory fibres and hence poor recovery would be expected in them. In other words, if the descending sympathetic fibres were found to be preserved, the chance for motor and sensory fibres to be intact are more. The findings of our study would contribute towards prognostication, for deciding on the rehabilitation programme and would help the patients and their relatives in terms of economy and anticipation.

Twenty four quadriplegic, traumatic spinal cord injury patients with lesion above T1, who were AIS grades A and B were recruited after informed consent, and their motor and sensory score at the time of admission were assessed. ECG data was acquired from them, followed by sympathetic skin response test. The data was analyzed to obtain resting heart rate and short-term HRV indices. The motor and sensory scores and the AIS grade of the patients was assessed again at the time of discharge, after completion of the routine rehabilitation programme and the change in scores was computed. The patients were also categorized into those who had good recovery (shifted into AIS grade C, D or E) and poor recovery (who remained in AIS grade A or B).

The short-term HRV indices obtained at the time of admission were studied for correlation with the change in motor and sensory scores at the time of discharge of the patients, with the aim of studying whether higher values of HRV indices would be able to predict a greater improvement in motor and sensory scores. The findings of sympathetic skin response were studied for association with poor and good recovery of the patients in terms of AIS grade.

Out of 24 patients studied, 10 were found have positive SSR and 14 patients had negative SSR. Of the 24 patients studied 5 patients alone showed good clinical recovery. The findings of our study showed no statistically significant correlation between short-term HRV indices and the change in motor score or sensory score. No statistically significant association was seen between the presence or absence of SSR at the time of admission and the clinical recovery pattern of the patients at the end of rehabilitation programme.

Thus the current study did not find short-term HRV indices and SSR to be useful parameters to prognosticate the recovery in traumatic cervical SCI AIS A/B patients. Assessment of autonomic functions through short-term HRV indices and SSR test provided no additional useful information to predict recovery pattern in AIS A/B cervical SCI patients in the present study.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

ANATOMY OF THE SPINAL CORD

The spinal cord or medulla spinalis is continuous rostrally with the medulla oblongata just below the level of the foramen magnum. It extends from the level of the upper border of the atlas to that of the lower border of the first lumbar vertebra. It terminates caudally as the conus medullaris, which is continous with the filum terminale.

The spinal cord is ensheathed by three protective membranes namely the dura mater, the arachnoid and the pia mater. The dura mater is separated from the wall of the vertebral canal by the epidural cavity. Between the dura mater and the arachnoid mater is the subdural cavity. The arachnoid is separated from the pia mater by the subarachnoid cavity. The cauda equine is a bundle of spinal nerves and spinal nerve roots, consisting of the second through fifth lumbar nerve pairs, the first through fifth sacral nerve pairs and the coccygeal nerve, all of which originate in the conus medullaris of the spinal cord. The filum terminale reaches as far as the lower border of the second sacral vertebra. The filum terminale is contained within the tubular sheath of dura mater, and is surrounded by the nerves forming the cauda equine.

SPINAL NERVES

The spinal cord consists of 31 segments, each have a motor and sensory nerve root. The sensory nerve root of the first cervical segment is very small and can be missing. These nerve roots combine to form 31 bilaterally symmetric pairs of spinal nerves (figure 1). There are eight pairs of cervical nerves, twelve thoracic, five lumbar, five

sacral and one coccygeal. Each nerve is attached to the spinal cord by a posterior root and an anterior root.

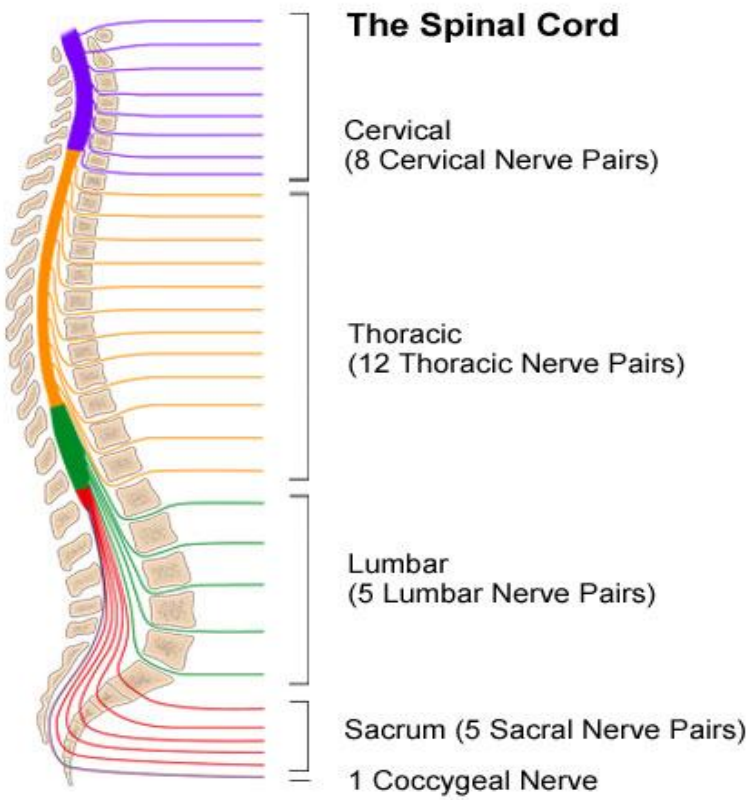

Fig.1. Spinal nerve root relation to vertebra.

The spinal cord is divided into two halves by a posterior median septum and a ventral median sulcus. It has an outer layer of white matter and an inner core of grey matter. It is largest by proportion in the cervical and lumbar regions since the amount of grey matter at any level is a function of the amounts of muscle, skin and other tissues innervated by the neurons at that level.

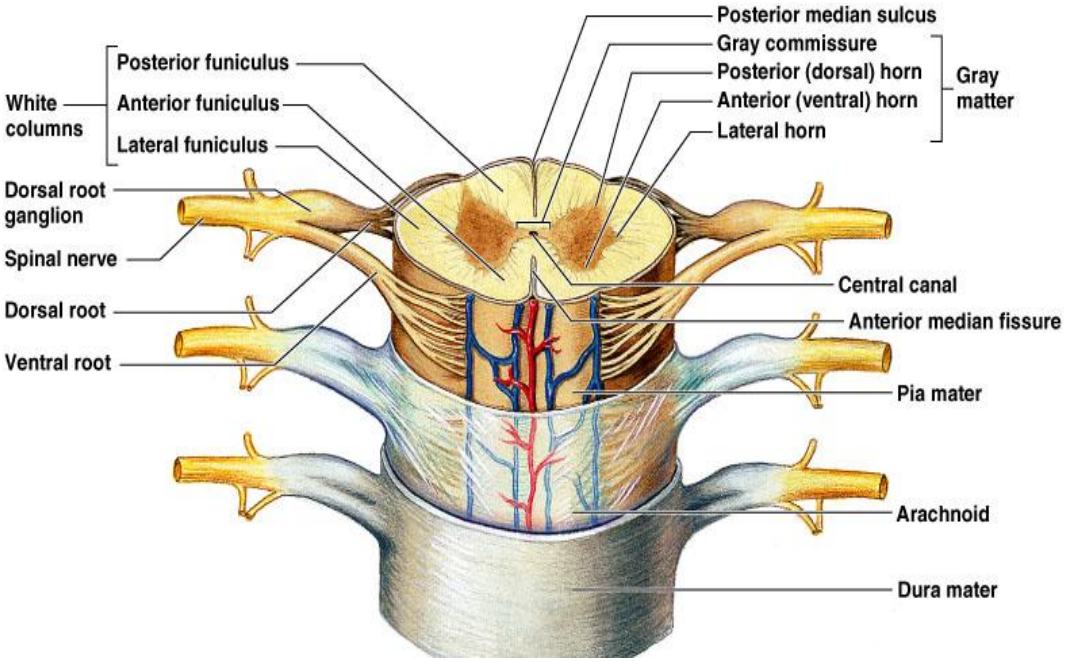

Fig.2. Cross section of the spinal cord and its nerves.

The spinal cord has four cellular masses namely two dorsal and two ventral horns which project dorsolaterally and ventrolaterally towards the surface (figure 2). The primary afferent fibres enter via the dorsal roots of spinal nerves and terminate in the dorsal horns. The ventral horns contain efferent neurons whose axons leave the spinal cord in ventral nerve roots. At the thoracic and upper lumbar levels, a small intermediate lateral horn is present which contains the cell bodies of preganglionic sympathetic neurons.

Dermatome is the area of skin innervated by the sensory axons within a particular segmental nerve root. Myotome describes the muscles innervated by a particular segmental nerve root.

ASCENDING AND DESCENDING PATHWAYS OF SPINAL CORD (figure 3)

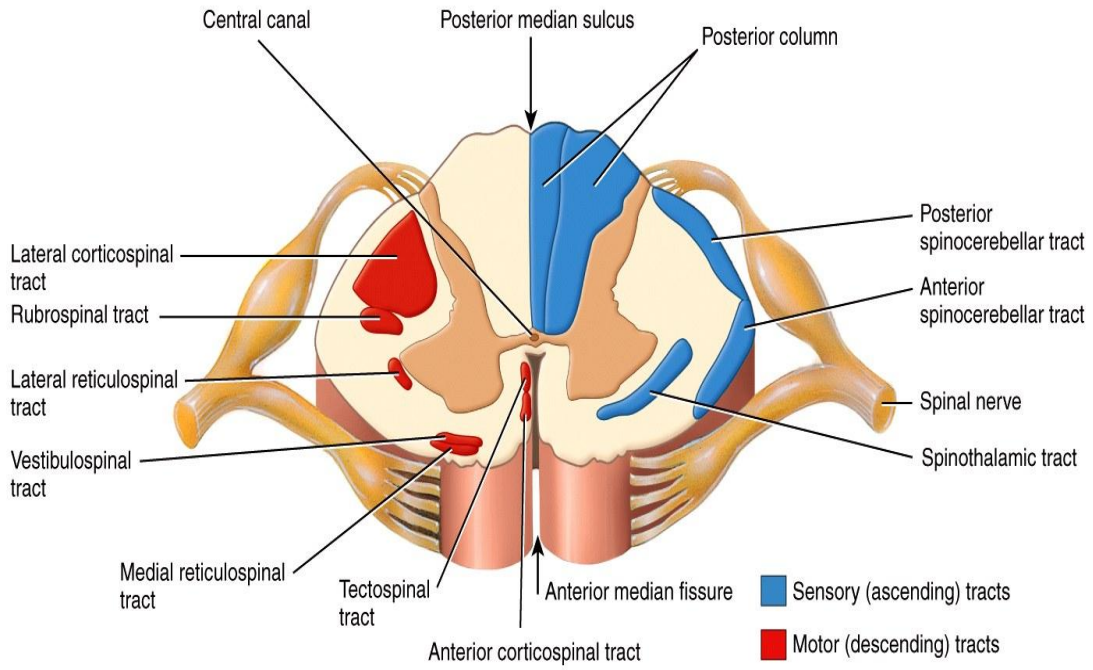

Fig.3. Cross section of the spinal cord with the ascending and the descending pathways.

MAJOR DESCENDING/MOTOR PATHWAYS

1. Anterior corticospinal tract
2. Lateral corticospinal tract
3. Rubrospinal tract
4. Lateral reticulospinal tract
5. Medial reticulospinal tract
6. Vestibulospinal tract
7. Tectospinal tract

MAJOR ASCENDING / SENSORY PATHWAYS

1. Posterior column - Fasciculus gracilis and Fasciculus cuneatus –
   Joint sense, position sense, vibration sense, fine touch, stereognosis and 2 point discrimination
2. Anterior and posterior spinocerebellar tract– posture and coordination
3. Anterior spinothalamic tract – Crude touch and pressure
4. Lateral spinothalamic tract - Pain and temperature.

BLOOD SUPPLY OF THE SPINAL CORD

The spinal cord is supplied by one anterior and two posterior spinal arteries. The anterior spinal artery arises from vertebral artery and supplies the anterior two third and central portion of the spinal cord. Ischemic injury to this vessel leads to dysfunction of corticospinal tract, lateral spinothalamic and autonomic intermedial pathways. The posterior spinal artery arises from posterior inferior cerebellar artery supplies the posterior one third of spinal cord and supplies mainly the dorsal column pathway. There are small spinal twigs from vertebral, ascending cervical, posterior intercostal and first lumbar artery. Artery of Adamkiewicz arises from aorta supplies the lower thoracic and lumbar cord.

There are six longitudinal venous channels, drained by the veins which leave the intervertebral foramen to empty in the lateral sacral, lumbar, posterior intercostals and vertebral veins. They connect with the cerebellar veins and cranial sinuses.

AUTONOMIC NERVOUS SYSTEM

The Autonomic nervous system is responsible for the regulation and integration of functioning of internal organs. The motor fibres of autonomic nervous system is classified into sympathetic and parasympathetic division.The preganglionic neurons of sympathetic fibres arise from intermediolateral horn of T1 to L3/L4 segment of spinal gray matter. The Preganglionic neurons of parasympathetic neurons arise from motor cranial nerve nuclei of III, VII, IX, X cranial nerves and Intermedio lateral horn of S2-S4 of spinal cord. Thus the sympathetic system has a thoraco-lumbar outflow, while the parasympathetic system has a cranio-sacral outflow. Acetylcholine is the neurotransmitter released by both preganglionic and postganglionic parasympathetic fibres. The preganglionic sympathetic fibres release acetylcholine while the postganglionic sympathetic fibres secretes norepinephrine except in sweat glands, blood vessels and in piloerector muscle, where it secretes acetylcholine.

The sympathetic preganglionic neurons receive supraspinal tonic and inhibitory nervous system control through spinal autonomic pathways, which are commonly disrupted in SCI. On the other hand, the cranial parasympathetic pathways which exit supraspinally, are intact in SCI. The heart is innervated by both the sympathetic supply from T1-T5 levels and the parasympathetic supply from the X cranial nerve, the vagus.

SPINAL CORD INJURY

HISTORY

The Sushruta Samhita, written in India during the third century A.D., describes the treatment of spinal cord injury. The care of cervical dislocations involved manipulative reduction, bandages, splints, and bed rest. Fractures of the lower spine were treated by immobilization, where the patient was placed on a board and tied down by ropes to five pegs. The authors of the Sushruta did not believe that spinal fractures were curable.(Lin & Cardenas 2003) The Edwin Smith papyrus, which dates to 3,000 to 2,500 years B.C. is the most authentic document, written by an Egyptian physician.(van Middendorp et al. 2010) Hippocrates (460–370 B.C.) created a method called succession on a ladder, as well as other methods of traction, for the treatment of spinal cord injuries. (Lin & Cardenas 2003) Donald Munro, Ernest H. J. Bors and Estin Comarr were the pioneers in the field of SCI.(Donovan 2007) The newer imaging techniques made the understanding and management of spinal cord injury easier.(Demaerel 2006) Later reports emphasized the advantages of surgical stabilization, early mobilization, prevention of further damage and speedy rehabilitation.(Ingelmo Ingelmo et al. 2010)

DEFINITION

Spinal Cord Injury (SCI) is generally defined as damage or trauma to the spinal cord that results in loss of function or impaired function. The term ‘Tetraplegia’ refers to impairment or loss of motor and/or sensory function of all the four limbs due to the damage of neural elements within the cervical segment of the spinal cord. C5 is the most common neurological level of injury in tetraplegics. The ‘Paraplegia’ refers to impairment or loss of motor and/or sensory function of both the lower limbs due to

damage of the thoracic, lumbar or sacral segments of the spinal cord. T12 and L1 are the most common levels in paraplegia.

EPIDEMIOLOGY

Globally, the incidence of spinal cord injury is found to be 1.7 lakhs per year. The incidence in Asia-Central and Asia-South is found to be 25 cases per million per year and 21cases per million per year respectively.(Lee et al. 2013) Automobile crashes are the leading cause of SCI until age 45 years, whereas falls from height are the leading cause after 45 years of age. The other causes are carrying heavy loads on the head, gunshot wounds, violence, motorcycle crashes, diving incidents and medical/surgical complications.(Chen et al. 2013)

In developed countries, low falls in the elderly are more common. In developing countries, low falls while carrying heavy loads on the head in the young people, high falls (from trees, balconies, flat roofs and construction sites), crush injuries, diving and violence are on the increase. Incidence of spinal cord injury in developing countries is found to be 25.5 cases per million per year.(Rahimi-Movaghar et al. 2013) Road traffic accident is the most common cause and fall from height the second most common cause of SCI in developing countries.(Chhabra & Arora 2012) As per the publication made by the Indian spinal injuries centre, New Delhi in the year 2012, the majority of the persons with SCI are males with the male to female ratio of 5.9:1. The mean age at the time of injury is 34 years.(Chhabra & Arora 2012)

ASIA IMPAIRMENT SCALE (AIS)

The spinal cord injury patients are classified based on American Spinal Injury Association (ASIA) Impairment Scale (AIS) (see Annexure IV). The different AIS grades are as follows:

A = Complete: No motor or sensory function is preserved in the sacral segments S4 - S5.

B = Incomplete: Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5.

C = Incomplete: Motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade less than 3

D = Incomplete: Motor function is preserved below the neurological level, and at least half of key muscles below the neurological level have a muscle grade of 3 or more.

E = Normal: motor and sensory function is normal.

Muscles of upper limb and lower limb were tested with the maximum score of 100 as in AIS grading.

0 = Total paralysis

1 = Palpable or visible contraction

2 = Active movement, full range of motion (ROM) with gravity eliminated

3 = Active movement, full ROM against gravity

4 = Active movement, full ROM against gravity and moderate resistance in a muscle specific position.

5 = (normal) active movement, full ROM against gravity and full resistance in a muscle specific position expected from an otherwise unimpaired person.

5* = (normal) active movement, full ROM against gravity and sufficient resistance to be considered normal if identified inhibiting factors (i.e. pain, disuse) were not present.

NT = Not Testable (i.e. due to immobilization, severe pain such that the patient cannot be graded, amputation of limb, or contracture of > 50% of the range of motion).

The pinprick and light touch sensation were tested with maximum score of 112(maximum) each.

Grade 0 – absent

Grade 1 – impaired

Grade 2 – normal

NT – not testable (if the patient is unconscious or in coma)

Both the motor and sensory score will be noted, when determining the AIS grade of a patient.

PATHOPHYSIOLOGY OF SPINAL CORD INJURY

Spinal cord injury is one of the most debilitating pathologies, leading to huge rehabilitation challenges. (Wu & Ren 2009) Primary injury occurs at the time of injury and secondary injury occurs due to compression or spinal instability. In both primary and secondary injury, injury to the blood vessels plays an important role. Various metabolites like seratonin, thromboxanes, platelet activating factor, calcium and potassium ions get accumulated and causes tissue injury. Apoptosis is an important event which occurs after SCI (Akdemir et al. 2008)

CONSEQUENCES OF SPINAL CORD INJURY

Spinal cord injured patients need to be treated immediately to prevent the consequences. (Chhabra& Arora 2013) Early admission of spinal cord injury patients reduces many complications like developing pressure ulcers, pneumonia and mortality compared to those with delayed admission. It was found that about 45% of complications can be prevented by early admission in specialized centers of care for spinal cord injury.(Parent et al. 2011) Cardiovascular complications are life threatening and are the major cause for death following SCI.(Julio C. Furlan & Michael G. Fehlings 2008)

The types of SCI are

1. Complete syndrome

2. Incomplete syndrome

- Central cord syndrome
- Brown sequard syndrome
- Anterior cord syndrome
- Posterior cord syndrome
- Conus medullaris and cauda equine lesion

COMPLETE AND INCOMPLETE SC SYNDROMES

The SCI may be complete or incomplete.

In Complete SC syndrome, there is total loss of motor and sensory function below the level of injury.

In Incomplete SC syndrome, there occurs partial loss of motor and sensory function below the level of injury with variable neurological findings. This includes central cord syndrome, brown sequard syndrome, anterior cord syndrome, posterior cord syndrome, conus medullaris and cauda equine lesion.

CENTRAL CORD SYNDROME

This occurs due to cervical or upper thoracic lesion of the spinal cord associated with motor weakness in the upper extremities, with sacral sparing. There is loss of pain and temperature sensation than proprioception.

BROWN SEQUARD SYNDROME

This occurs due to hemisection lesion of the spinal cord. It is associated with ipsilateral loss of motor function and proprioception and contralateral loss of pain and temperature sensation. Here, patients often have good prognosis. (Pribán & Fiedler 2010)

ANTERIOR CORD SYNDROME

This syndrome occurs when the blood supply to the anterior portion of the spinal cord is interrupted. It is associated with loss of motor function and pain and temperature sensation. But touch sensation, proprioception and vibration sensation remain intact.

POSTERIOR CORD SYNDROME

This is associated with the loss of proprioception (leads to ataxia), astereognosis and graphaesthesia. Motor function, pain and touch sensation remain intact.

CONUS MEDULLARIS AND CAUDA EQUINE LESION

Conus medullaris lesion is a sacral cord injury. It is associated with areflexia in the bladder, bowel and lower limbs. Bulbocavernous and micturition reflexes may be preserved. Motor and sensory functions in the lower limbs are variable.

Cauda equine lesion involves lumbosacral nerve roots. It is associated with areflexia of bladder, bowel and lower limbs. Motor and sensory function loss is variable.

Consequences of spinal cord injury other than motor and sensory dysfunction are:

- Neurogenic shock
- Spinal shock
- Autonomic dysreflexia
- Orthostatic hypotension
- Neurogenic bowel
- Psychiatric symptoms
- Respiratory dysfunction
- Micturition disturbances

NEUROGENIC SHOCK

Severe hypotension and persistent bradycardia are common in neurogenic shock. This can last up to 5 weeks after injury which requires vasopressor therapy to maintain systolic arterial blood pressure above 90 mmHg. Intact vagal nerve and loss

of sympathetic tone due to disruption in supra spinal control leads to loss of vascular tone.

SPINAL SHOCK

It is characterized by a marked reduction or complete loss of motor and reflex function (aflexia and hypotonia) below the level of injury. It lasts upto4 to 6 weeks of post injury. Bulbocavernous reflex is the first reflex to return followed by deep tendon reflex and bladder reflex.(Ditunno et al. 2004)

AUTONOMIC DYSREFLEXIA

Autonomic dysreflexia occurs if the spinal sympathetic centers are disconnected from the higher centers.(Curt et al. 1996)

It is a condition of episodic hypertension with systolic blood pressure reaching up to 300mmHg, associated with pounding headache, slow heart rate and upper body flushing.(Weaver & Polosa 2005) The serious consequences if left untreated include intracranial hemorrhage, retinal detachment, seizure, cardiac arrhythmias, and death. Various noxious and non-noxious stimuli like bowel and bladder distension, procedures like catheterization, cystoscopy, cystometry, vibration or electro stimulation for ejaculation as well as electro stimulation of muscles, urinary tract infection can trigger this condition. Sometimes, it may not be so severe even in quadriplegic and may be associated only with sweating and piloerection.

ORTHOSTATIC HYPOTENSION

The American Academy of Neurology defined Orthostatic Hypotension as a decrease in systolic pressure of more than 20mmHg, or a decrease in diastolic pressure of more than 10 mmHg, on assuming the upright posture from supine posture. Patients

with high SCI experience drop in blood pressure in addition to low resting arterial pressure. It may also be due to excessive pooling of blood in the lower extremities and the abdominal viscera. (Krassioukov et al. 2009) Low plasma volume, hyponatremia and cardiovascular de-conditioning due to prolonged rest are the possible causes. The prevalence of orthostatic hypotension is more common in tetraplegia.(Sidorov et al. 2008)

NEUROGENIC BOWEL

Adynamic ileus, prolonged total gastrointestinal transit time occurs commonly during the acute phase of SCI, due to loss of both sympathetic and parasympathetic supply (parasympathetic supply from sacral segments of the spinal cord) during the neurogenic shock.(Benevento & Sipski 2002) Nausea, vomiting, belching, hiccups, constipation, fecal incontinence, obstructive defecation which may be due to loss of sympathetic activity which is one of the essential components in coordination of gastrointestinal peristalsis. (Chen et al. 2004)

Inability to control the bladder and bowel function affects emotional and social life of these individuals.

PSYCHIATRIC SYMPTOMS

SCI patients are prone for post traumatic stress, depression and anxiety (O'Donnell et al. 2013)

RESPIRATORY DYSFUNCTION

Death is common following spinal cord injury and the leading cause is failure of the respiratory system.(van den Berg et al. 2010) Loss of ventilator muscle function due to denervation or chest wall injury, decreased central ventilator drive due to head

injury or lung injuries such as pneumothorax and hemothorax contribute to respiratory dysfunction.

MICTURITION DISTURBANCES

Bladder areflexia causes urinary retention which is common during the acute phase of SCI. The patients are catheterized to prevent bladder overstretching. After the spinal shock, due to disruption of descending spinal pathways, coordinated voiding is lost. A spinal micturition reflex emerges during the recovery which mediates involuntary or automatic micturition.

RECOVERY FOLLOWING SCI

Mortality following spinal cord injury has declined of recent times because of the improvement in the treatment during the acute phase and the follow up rehabilitation. There will be an initial period of spinal shock following spinal cord injury which may last for four to six weeks. Bulbocavernous reflex is the first to return followed by deep tendon reflexes and bladder reflex. Though the research to cure SCI is encouraging, currently there is no proven way to restore the function fully following SCI.

Functional motor recovery is ability to move a joint through its full range of motion against the gravity (Grade 3/5 strength). In fact, there is no proven way to predict the recovery with 100% accuracy. So far, the recovery is predicted on whether the injuries are complete or incomplete with the AIS scale.

In a study by Waters et al in 1993, in complete tetraplegia, despite the initial neurological level of injury between C4 and C8, the amount of motor and sensory recovery was found to be independent. The average increase in the motor score

between one month and one year was found to be 8.6±4.7.(Waters et al. 1993) The rate of motor recovery declines during first 6 months and attains plateau. In a study by Waters et al in 1994, in incomplete tetraplegia with bilateral sacral sensation, between one month and one year following injury, the average increase in the motor score in the lower extremity was 12.1±7.8 at one year. The rate of recovery rapidly declined in the first 6 months.(Waters et al. 1994)

In another study by Fisher et al 2005, the motor recovery did not occur below the level of injury in complete tetraplegic patients but, local neurological recovery in the zone of partial preservation was observed. The average AIS motor score was 11.9±10.7 on admission and 20.1±10.8 at the time of follow-up at 2 years and this change was due to local recovery.(Fisher et al. 2005)

In a study by Marino et al, 3.6% of AIS A patients shifted to AIS C at the time of discharge and 36.8% and 17.8 % of AIS B patients shifted to AIS C and AIS D respectively at the time of discharge. (Marino 2007)

So far, there is no treatment available to improve the recovery in spinal cord injured patients. Even if the regenerating axons are used for the target neurons as a trial, the recovery of function will be limited and show no real increase in the quality of life. (Ellaway et al. 2004)

The International Spinal Research Trust (ISRT) in 2001 aimed at developing a wide range of clinical and physiological tests for assessing the boundaries and density of SCI and for monitoring of recovery over one or two spinal segments. The present neurological assessment criteria (AIS impairment scale) ignore the muscles innervated by thoracic spinal cord segments and did not include the tests of cardiac, vasomotor and sudomotor autonomic functions. New improved tests of function are

therefore needed to assess the density of spinal cord lesions above and below the level of injury.

Since autonomic dysfunctions with abnormal cardiovascular control are common consequences following spinal cord injury, there is a need to include international SCI cardiovascular function basic data set and autonomic function tests to the International SCI Core Data Set. (Krassioukov et al. 2009) To improve the evaluation of autonomic function in spinal cord injured patients and in the future to assess the effects of therapeutic interventions, the ASIA and International Spinal Cord Society (ISCoS) established a committee to develop a set of definitions and classifications for autonomic function disorders in SCI. (Marino 2007)

In a study by Katoh and el Masry, to predict the degree of motor recovery in spinal cord injured patients, the preservation of the sensation between the level of injury and the sacral dermatomes was considered. (Katoh & el Masry 1995) But, some patients with preserved sensation did not recover.

At the time of admission of a SCI patient, the question uppermost in the minds of both doctors and patients is the extent to which the patient will recover. There is no proven way to assess the prognosis of motor and sensory recovery in SCI patients. In the present study, autonomic function tests were assessed in the SCI patient at the time of admission for rehabilitation, with the aim of gauging the intactness of descending autonomic control. It was then studied whether the parameters of autonomic function had any relation with subsequent motor and sensory score.

HEART RATE VARIABILITY INDICES

Sino Atrial node, the pacemaker of the heart receives both the sympathetic and parasympathetic supply. (figure 4) Physiological beat-to-beat variations in heart rate are largely modulated by efferent vagal and sympathetic outflow. Both the sympathetic and vagal activity fluctuates continuously due to fluctuation of various inputs like respiration and baroreceptor inputs (Zygmunt & Stanczyk 2010) resulting in beat-to-beat variations of the heart rate. This variation in milliseconds of cycle length between adjacent cardiac cycles or RR intervals is known as Heart Rate Variability (HRV).

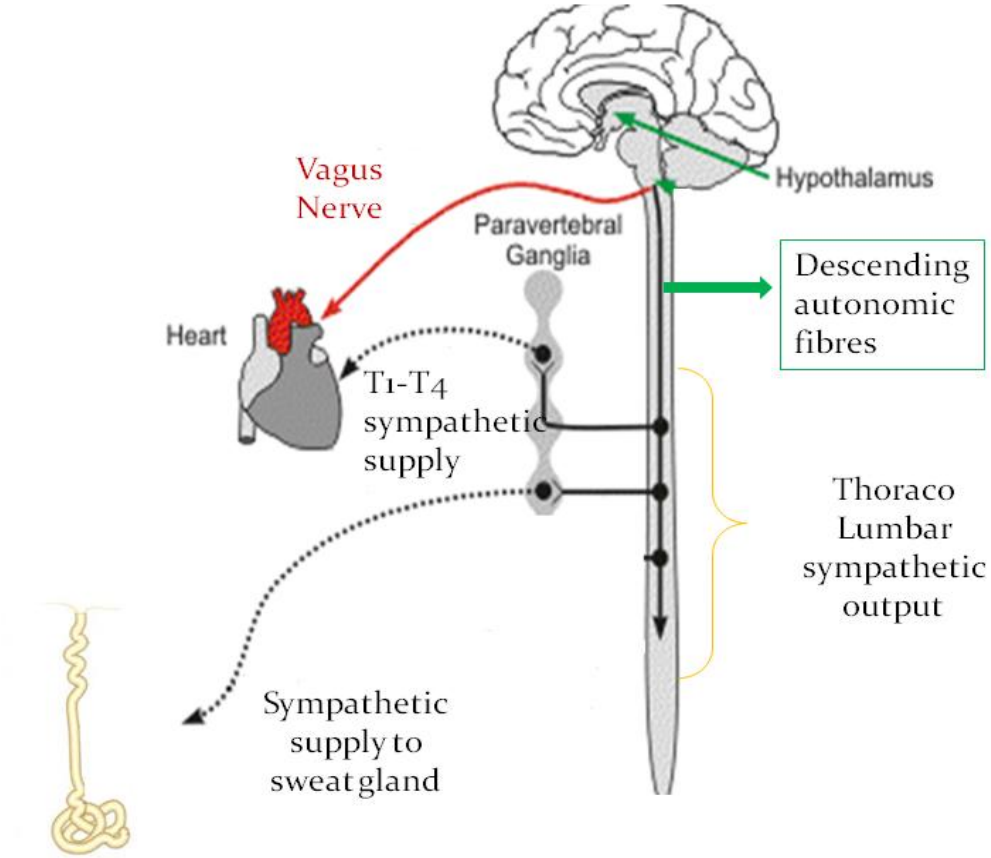

Fig.4. Overview of autonomic pathways.

The normal heart rate in an adult is 60 to 80 beats per minute. The Intrinsic firing rate of sino atrial node is 100 - 110 beats per minute. In normal adult, vagal tone and vagal inhibition is more than the sympathetic tone. So, the resting heart rate is less than the intrinsic firing rate.

The heart rate increases during inspiration and decreases during expiration. The change in the heart rate due to respiration has been termed as respiratory sinus arrhythmia (Hirsch & Bishop 1981) which is an important component of normal HRV. This is due to the influence of stretch receptors located in the lungs, chest wall, heart and the vessels on efferent vagal neurons in the medulla, that innervate the heart. (Freyschuss& Melcher 1976)

Vagal pulmonary stretch receptors modulate the efferent outflow to the sinus node. Inspiration increases venous return stretching atrial receptors, which produces an increase in afferent traffic to the medulla which result in vagal withdrawal and increase in heart rate. While, expiration decreases venous return and heart rate slows. Vagal cardioinhibitory motor neurons of the nucleus ambiguous receive a powerful inhibitory input throughout inspiration and are excited in the early expiratory phase. (Shykoff et al. 1991) Respiration alters the reflexes from pressure baroreceptors. (Freyschuss & Melcher 1976)

The influence of parasympathetic activity is quick and transient due to fast degradation of acetylcholine by acetylcholine esterase. Hence, the effects of parasympathetic activity are visible in the next cycle after the stimulus and the parasympathetic nervous system accounts for quick changes in heart rate. Changes in the heart rate due to changes in sympathetic activity develop slowly and the effects are visible only after 2-3 seconds. Thus sympathetic activity contributes to the slower oscillations in the RR intervals.

Measuring HRV is easy and provides sensitive, specific and reproducible measures of cardiac vagal function. (Vinken& Bruyn 1999) Resting HRV, an index of sympathetic and parasympathetic cardiac outflow, is determined in the subjects in supine position as heart rate fluctuations may be more pronounced in this posture. Short-term HRV is assessed from 5 minutes of ECG recordings, while the long term HRV is assessed from 24 hours of Holter ECG recording.

Each RR interval denotes the duration of one cardiac cycle. By computing RR intervals from the recorded ECG (figure 5), HRV can be analyzed using specific softwares. Various softwares and algorithms are used to derive the time domain and frequency domain indices of short-term HRV from the RR intervals. (Kuo & Chen 1998)

Mean RR interval is the measure of average of all normal to normal (NN) RR intervals. It is an indicator of sympathovagal balance as mean RR is inversely proportional to the heart rate.

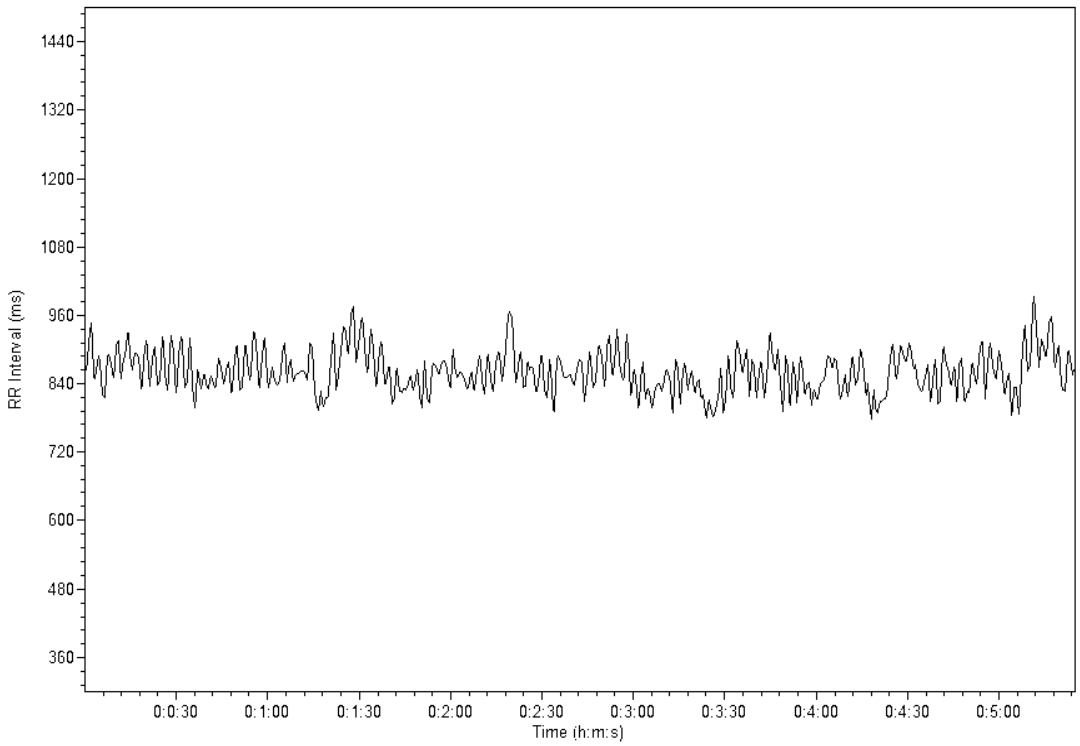

Fig.5. RR interval tachogram from an ECG recording with time on x-axis and RR interval on y-axis.

The HRV can be quantified by using time domain and frequency domain analysis.

TIME DOMAIN ANALYSIS

1. SDNN – Standard deviation of all normal to normal RR intervals. It is a measure of total variability, which include variability due to sympathetic and parasympathetic modulation and reflects the sum of HRV in low and high frequency ranges.(Stein, PhD & Kleiger, MD 1999) (Electrophysiology 1996)

2. RMSSD – Square root of mean squared difference of successive normal-to-normal RR intervals. If the difference between RR intervals is more, the parasympathetic modulation is more. (Stein, PhD & Kleiger, MD 1999)

3. pNN50 – Proportion of differences in consecutive normal-to-normal RR intervals that are longer than 50 ms. It estimates high frequency variations.(Zygmunt & Stanczyk 2010)

FREQUENCY DOMAIN ANALYSIS

Frequency domain analysis can be done by using mathematical algorithms like fast fourier transformation (FFT). RR interval tachogram biosignal has to be decomposed into its component frequencies and the power in each frequency band is estimated. ECG wave is composed of different frequencies. Similarly the RR interval tachogram is also composed of different frequencies. FFT mathematically teases out these different component frequencies in the RR interval tachogram and displays frequencies on X axis and its power on Y axis (figure 6). Power of specific frequency bands depends on extent of modulation of sympathetic and parasympathetic supply on heart.

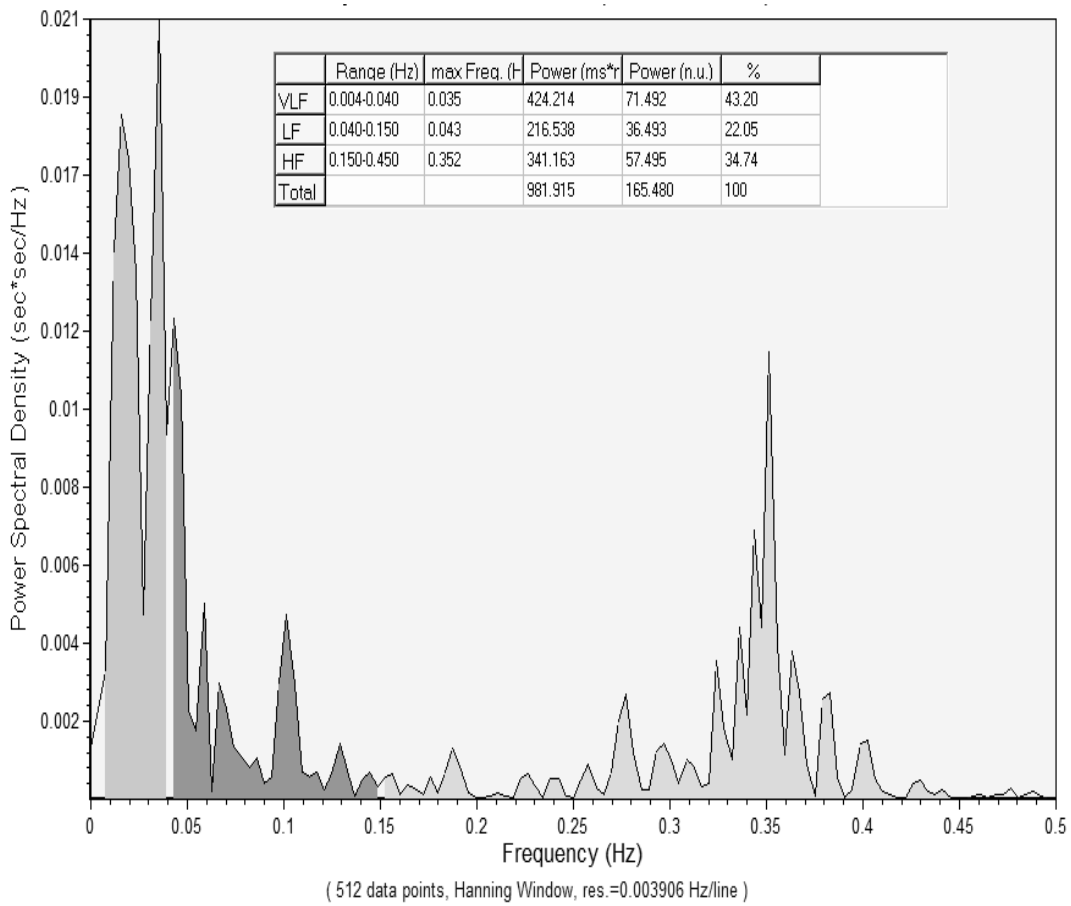

Fig.6. Output of the power spectral analysis of the RR interval tachogram using fast fourier transform giving the distribution of the power across the frequency. X axis = frequency, Y axis = power spectral density.

Following are the parameters obtained by frequency domain analysis:

1. HF (High Frequency) power:

   Power in ms^2 in the range of 0.15 – 0.4 Hz produced by parasympathetic modulations; modulations of RR intervals by respiratory sinus arrhythmia falls in this band. (Malliani et al. 1994)

2. LF (Low Frequency) power:

   Power in ms^2 in the range of 0.04-0.15Hz, by sympathetic and parasympathetic modulations. (Electrophysiology 1996) (Malliani et al. 1994)

3. VLF (Very Low Frequency) power:

Power in ms^2 in the range of < 0.04Hz, which may be due to body temperature fluctuation or hormonal fluctuations like renin-angiotensin-aldosterone axis.

4. Total power:

   It is the sum of VLF, LF and HF power in ms^2. It denotes the total variability in long term HRV analysis.

5. LF+HF power:

   It is the equivalent of total power in Short-term HRV analysis and is the sum of LF and HF powers. It denotes the total variability in short term HRV analysis and denotes the sum of sympathetic and parasympathetic modulations.

6. LF nu and HF nu:

   LF nu (normalized unit) is the ratio of LF power to sum of LF and HF power and HF nu is ratio of HF power to sum of LF and HF power. Expression in normalized units decreases the effect of changes in total power due to changes in VLF powers on these ratios and shows the balance of both the sympathetic and parasympathetic system.

7. LF/HF ratio:

   Ratio of sympathetic modulation to vagal modulation, reflects the sympathovagal balance.(Zygmunt& Stanczyk 2010)

HRV IN CERVICAL SPINAL CORD INJURY PATIENTS

In quadriplegic patients with a complete spinal cord lesion above T1 spinal segmental level, the cardiac sympathetic pathway which originates from T1-T4 segments, will lose its control from the higher brain centres. This will alter the sympathetic drive to the heart. But, the parasympathetic supply to the heart will be intact. Hence, the HRV indices get altered in spinal cord injury patients. (Claydon& Krassioukov 2008)(Grimm et al. 1997)

Reports on the LF component in quadriplegic is inconsistent. According to Inoue et al, only HF component is seen in quadriplegic. Even if LF component is seen, the central frequency of the LF component was lower than in normal healthy subjects. (Inoue et al. 1995) LF component is reported to be lower in quadriplegic and in paraplegic than in normal subjects predominantly because of sympathetic denervation. (Bunten et al. 1998) The HF component is also reported to decrease in quadriplegics. This is attributed to the decrease in parasympathetic activity to the heart which occurs to match the loss of sympathetic stimulation of the heart, thus maintaining the autonomic stability. (Grimm et al. 1997)

Heart rate, LF, LF: HF ratios are highly reproducible while HF is less reproducible in tetraplegics. Hence, HRV indices can be used as reproducible indices of autonomic cardiovascular regulation in these patients. (Ditor et al. 2005) LF to HF ratio is normal which indicates that the sympathovagal balance is maintained in chronic spinal cord injury patients. (Wang et al. 2000) The time domain variables like SDNN, RMSSD, pNN50 are decreased in patients with chronic spinal cord injury during night time and SDNN is decreased during day time.

LF which represents sympathetic activity has negative correlation with orocaecal transit time which indicates the gastrointestinal peristalsis in quadriplegic patients who have severe gastrointestinal symptoms (nausea, vomiting, belching, constipation). (Chen et al. 2004) HRV can be used as a predictor of risk after acute MI and as an early warning sign of diabetic neuropathy. (Electrophysiology 1996) During mental stress, the mean RR interval decreases associated with a decrease in total heart rate variability which has to be considered while evaluating HRV in patients. (Tharion et al. 2009)

MECHANISM OF SWEAT PRODUCTION

There are three types of sweat glands – eccrine glands, apocrine glands and apoeccrine glands. The apocrine glands arise from hair follicles and are found mainly in the axillae, around the nipples, pubic region and on the skin of abdomen. The eccrine glands is the primarily responsible for thermoregulatory sweating in humans.(Shibasaki et al. 2006) There are two types of eccrine glands present in the human skin – those which are concerned with temperature regulation are distributed on the body surface and those which respond to mental, emotional(Kamei et al. 1998) and sensory stimuli stress are located on the palms, soles and forehead. The sweat glands arise from the epidermis proper and are widely distributed throughout the body. It has secretory coil (which produces the sweat) and a duct. The sympathetic nerve terminals are found mainly around the secretory coil of the sweat gland and also extend to the duct.

Normal thermoregulation depends mainly on the presence of intact sympathetic pathway. Sweat testing provides a means of gauging the function of the sympathetically innervated eccrine sweat glands. The exact neurological pathway for sweat production is not clearly understood. The efferent pathway from the preoptic nucleus of hypothalamus travels through the tegmentum of pons and medullary raphe on the same side to reach the intermediolateral horns of the spinal cord. Pre-ganglionic sympathetic fibres arise from intermediolateral horn cells and exits through the ventral horn to synapse in the sympathetic ganglia. The postganglionic non myelinated C fibres arising from these sympathetic ganglia, join the peripheral nerve fibres and travel to the sweat glands.(Nakamura 2004) Acetylcholine is the neurotransmitter at the neuroeffector junction between the sympathetic supply and sweat glands and causes sweat production.

SYMPATHETIC SKIN RESPONSE

The sympathetic skin response (SSR) is an intersegmental, multisynaptic, somato-sympathetic reflex. It is the recording of the change in electrical skin potentials produced by changes in sweat production, in response to a variety of stimuli. The response can be obtained directly by stimulating a peripheral nerve or reflexly by other modes of stimulation, all of which activate the sympathetic supply to the sweat glands, increasing sweat production and altering the skin electrical potential. Electrical stimulation of median nerve, peroneal nerve (Cariga et al. 2002), electrical stimulation of supraorbital nerve of forehead, tibial nerve and umbilical region (Ogura et al. 2004), sudden loud noise, inspiratory gasp (Vinken& Bruyn 1999), visual stimuli (Nagarajarao et al. 2006) emotional or magnetic stimulation (Chroni et al. 2006) can produce SSR. These stimuli elicit a diffuse intersegmental response via sympathetic nerves.

SSR is most frequently used in diagnosing the functional impairment of non-myelinated post ganglionic sudomotor sympathetic fibres in peripheral neuropathy. The phenomenon of changes in skin potential following stimulation of special senses was first described by Tarchanoff. (Tarchanoff 1890) It is a result of polysynaptic reflex arc activation. The method of SSR recording was introduced into practice in electrophysiological laboratories by Shahani in 1984 (Shahani et al. 1984) and later by Knezevic and Bajada in 1985.

SSR can be recorded on most EMG machines. The potential has low frequency content, therefore, low frequency filters should be set at 0.1 or 0.5 Hz, high frequency filter at 500 to 1000 Hz & gain to record a potential of 0.5-3mV & sweep to record 5s after the stimulus of 10 to 50 mA. (Uk& Al 2006) The recordings are obtained simultaneously from the hands & feet. SSR can also be recorded on a single channel

ECG recorder by connecting the electrodes on hands and feet. (Nagarajarao et al. 2006)

SSR can be used to assess the integrity of sympathetic pathway (afferent fibres from the higher centres in the brain to the intermediolateral horn cells in spinal cord and efferent fibres out through the pre- and then post ganglionic sympathetic fibres) in spinal cord injury patients. (Ogura et al. 2004) (Cariga et al. 2002) (Nagarajarao et al. 2006) The pre and post ganglionic sympathetic fibres are expected to be intact in SCI patients, so that the SSR gives information about the presence or absence of the higher neural control of the spinal sympathetic sudomotor outflow.

In hands, active electrodes are placed on the palm of hand and reference electrodes are placed on the dorsum of the hand. In feet, active electrodes are placed on the sole and reference electrodes are placed on the dorsum of the feet. (figure 7)

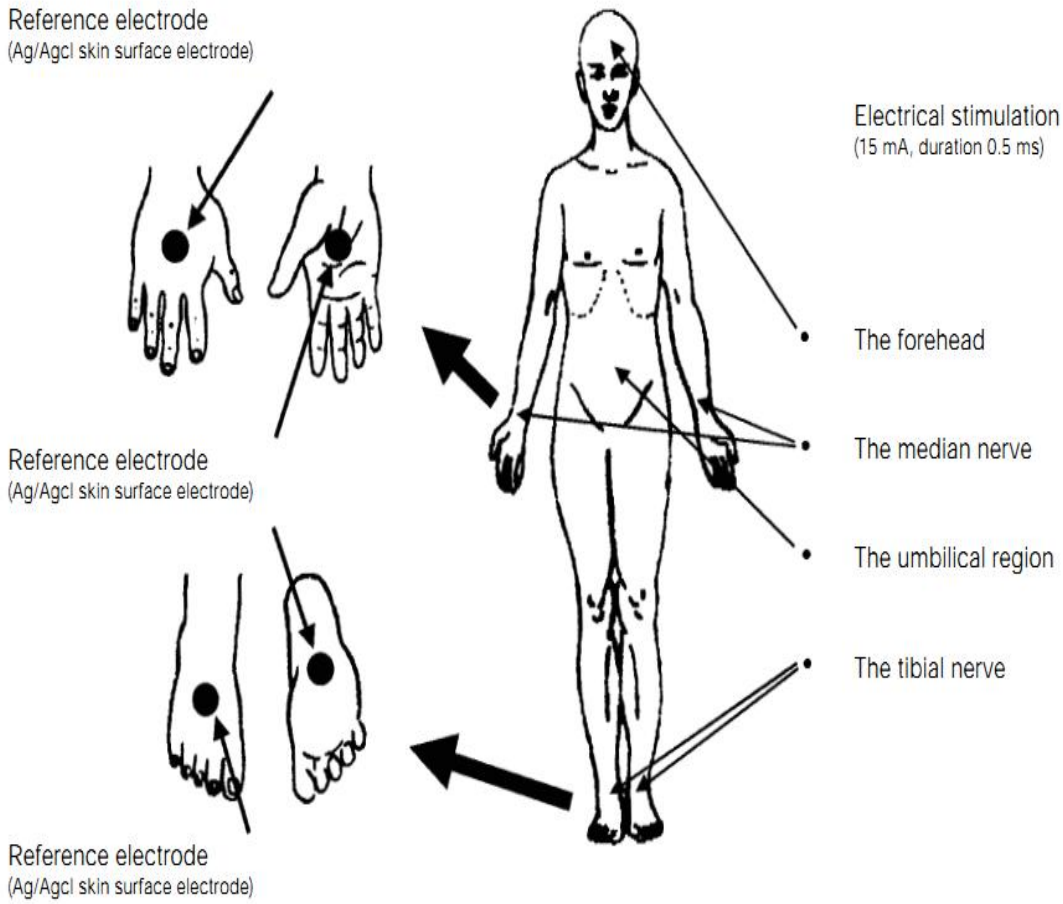

Fig.7. Electrode placement in palms and soles and areas of electric stimulation.

On repetitive stimulation to elicit the SSR, the SSR amplitude decreases. This is known as habituation of the SSR. The habituation depends on the number of stimuli. If the stimulus is applied at 1 min interval, habituation is not seen. Habituation can be reverted back if the stimulation is altered from electric to magnetic stimuli. (Toyokura 2006)

AIM AND OBJECTIVES

AIM

To study the relationship between initial autonomic functions in quadriplegic patients with traumatic spinal cord injury and subsequent motor and sensory recovery.

OBJECTIVES

A. To assess the following variables in acute cervical spinal cord injury patients before rehabilitation therapy.

1. Resting heart rate
2. Resting respiratory rate
3. Short-term Heart Rate Variability indices
4. Sympathetic skin response

B. To compute the change in Motor and Sensory score and the AIS grade of the spinal cord injury quadriplegic patients at the end of the routine rehabilitation programme from that recorded before the start of the rehabilitation programme.

C. To study the correlation between short-term heart rate variability indices and the change in motor and sensory score at the end of the rehabilitation programme.

D. To study the association between presence or absence of sympathetic skin response and subsequent motor and sensory recovery at the end of the rehabilitation programme.

MATERIALS AND METHODS

SUBJECTS

Traumatic cervical spinal cord injury patients admitted for rehabilitation under the department of Physical Medicine and Rehabilitation of the institute were recruited into the study.

INCLUSION CRITERIA

Quadriplegic patients with traumatic spinal cord injury with lesion above T1 with AIS grades A and B were included.

Since the cardiac autonomic fibres arise from the T1 to T4 spinal segments, patients with lesion above T1 alone were included, as the objective of the study was to study the integrity of the higher centre autonomic control of the cardiac sympathetic fibres. Patients of both gender were included.

EXCLUSION CRITERIA

Quadriplegic patients with progressive spinal cord injury due to diseases like syringomyelia and tumours, quadriplegic patients with lesion involving T1 to T4 spinal segments and patients with cardiac pacemaker were excluded.

TYPE OF STUDY

This was a Prospective Cohort study.

SAMPLE SIZE CALCULATION

From a previous study, it was known that the initial motor score in quadriplegic SCI patients was 38.2±30 and the motor score after rehabilitation was 56.7±31.7.

Applying the Single Mean Paired t-test, with a power of 80% and alpha error of 5% a sample size of 24 subjects was obtained.

RECORDING OF MOTOR AND SENSORY SCORES AND THE AIS GRADE

The initial motor and sensory scores and AIS grades of the patients were recorded by physicians of the PMR department at the time of admission of patients. The process of assessing the motor and sensory scores and the AIS grading were repeated again after routine rehabilitation programme in the rehabilitation centre, just before the patients were discharged. The physicians who scored the motor and sensory scores and graded the patients into the AIS grades were blinded to the outcome of the SSR test and to the results of the short-term HRV analysis. Motor and sensory score and AIS grade were assessed according to the protocol of American Spinal Injury Association.

RECORDING OF SSR AND SHORT-TERM HRVANALYSIS

The SSR test and the recording of ECG for HRV analysis were done on the patients as soon as they were hemodynamically stable (vital signs – heart rate and blood pressure became stable) after admission. Those patients who were on anticholinergic drugs were taken off the medication for four days prior to the day of testing. Test was done after obtaining the informed consent from them.

PRETEST INSTRUCTIONS

Patients recruited into the study were informed about the instructions to be followed prior to the day of recording of the SSR and the ECG for HRV analysis. None of the patients consumed alcohol or nicotine prior to the day of the recording. The patients were instructed to not consume any food for 3 hours prior

to the time of recording. The patients were encouraged to have a sleep of at least seven hours in the previous night. The instructions were to avoid caffeinated beverages for 12 hrs prior to the time of the recording.

EXPERIMENTAL PROTOCOL

All the experiments were done in a quiet room in which the room temperature was maintained at 24-26 ºC, since room temperature can affect the outcome of SSR. (Kucera et al. 2004) All the recordings were obtained between 11 a.m. to 2 p.m.

The experiments were done in the following order after ten min of rest period:

1. Recording of 5 min ECG for short term HRV analysis.
2. Sympathetic skin response test by blast sound.
3. Sympathetic skin response test by electrical stimulation.

INSTRUMENTATION

The sympathetic skin response and the ECG for HRV analysis were obtained by using a custom made data acquisition system, the CMCdaq, developed by the department of Bioengineering, Christian Medical College, Vellore (figure 8 & 9). The analog signals were digitized at a sampling rate of 1000 Hz and acquired using the CMCdaq software into the PC and stored.

Fig.8. Four channel CMCdaq.

Fig.9. Eight channel CMCdaq.

DATA ACQUISITION

With the subject lying supine on the bed, instrumentation was done. ECG leads were placed in lead II configuration after cleaning the skin with cotton soaked with spirit.

Repeated measurements of blood pressure (BP) were made by manual sphygmomanometry using a mercury sphygmomanometer till a stable blood pressure was obtained. After a rest period of ten minutes, five minutes of ECG recording was done. The ECG was amplified and converted to digital signals (figure 10) and stored in a personal computer using the CMCdaq.

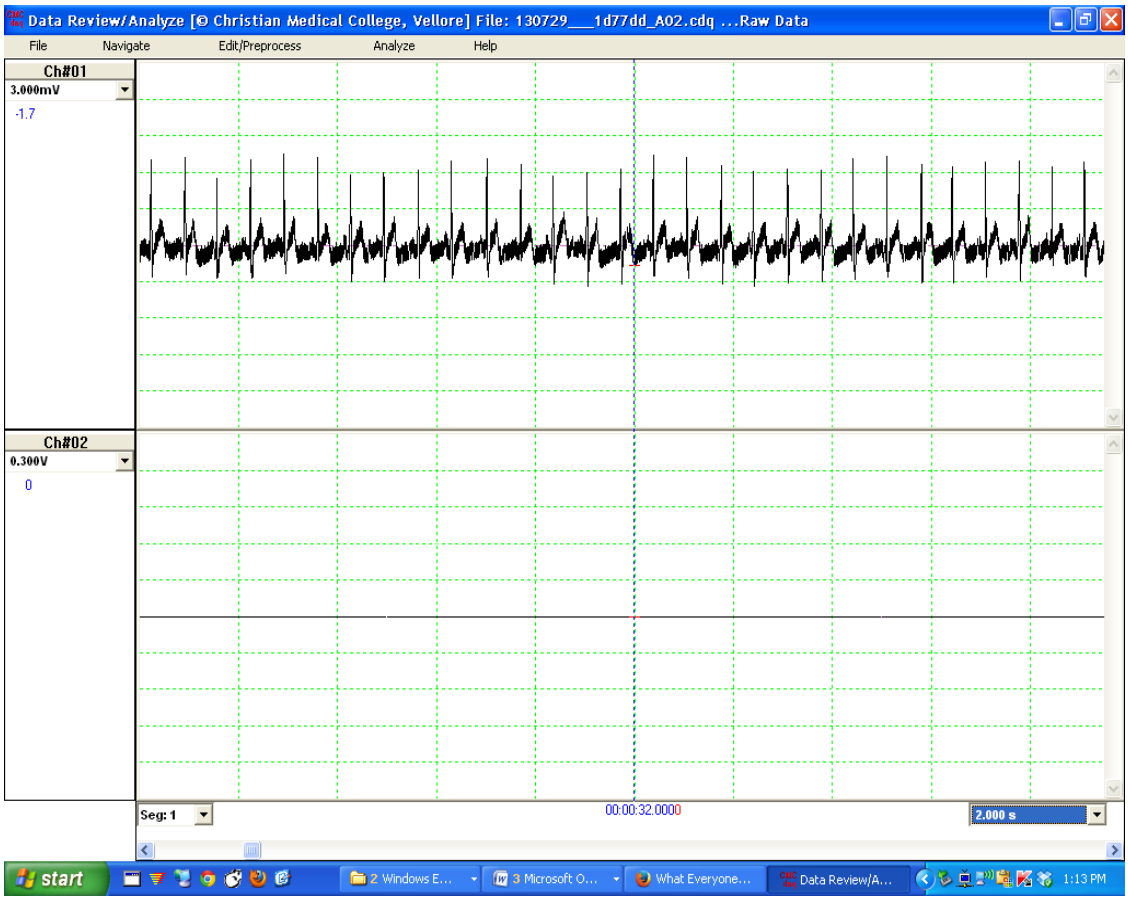

Fig.10. ECG (in first channel) recorded in a cervical cord injury patient.

The resting heart rate was calculated from the 5 min of ECG recording. The mean arterial pressure was calculated from the resting blood pressure. Resting respiratory rate was counted manually by noting the abdominal movements during the 5 min of ECG recording.

SHORT- TERM HEART RATE VARIABILITY ANALYSIS

Short term HRV analysis was done offline using the recorded ECG as per the guidelines published by the task force on HRV analysis. (Electrophysiology 1996) The 5-minute ECG was scrutinized to ensure that there were no ectopic beats and no artifacts and noise. Using CMCdaq software, the peaks of R wave were selected (figure 11).

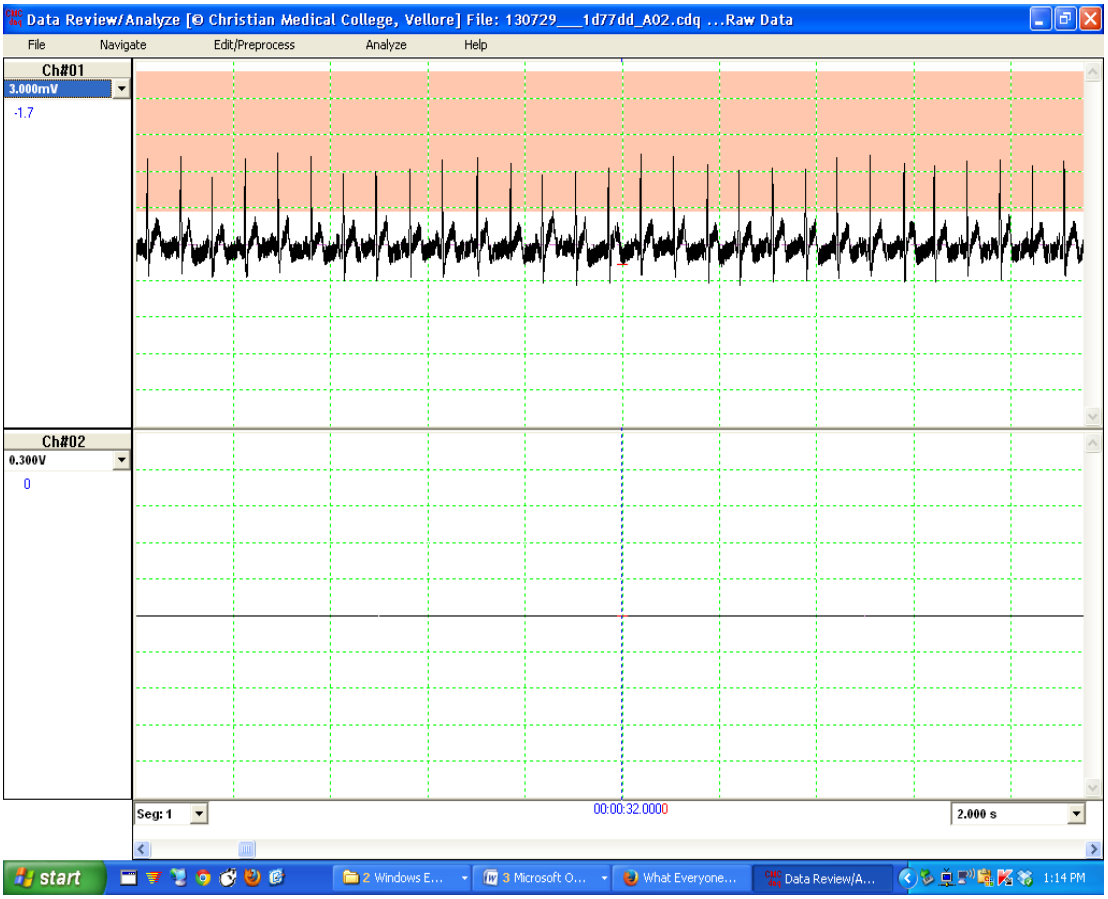

Fig.11. HRV analysis in a cervical cord injury patient.

This program calculated the RR interval and gave as a text file. These RR intervals were then fed into Microsoft Excel and the RR intervals were copied into a Notepad file.

By feeding this 5-min RR interval notepad file into HRV analysis software, Nevrokard aHRV ver.12.0.0 (Medistar, Solvenia), RR interval tachogram was obtained which is a plot of the RR intervals on the y axis and the time of occurrence of R waves on the x axis (figure 12). Further, the software computed the time and frequency domain parameters from the tachogram.

The time domain parameters computed were coefficient of variance, SDNN, RMSSD and pNN50.

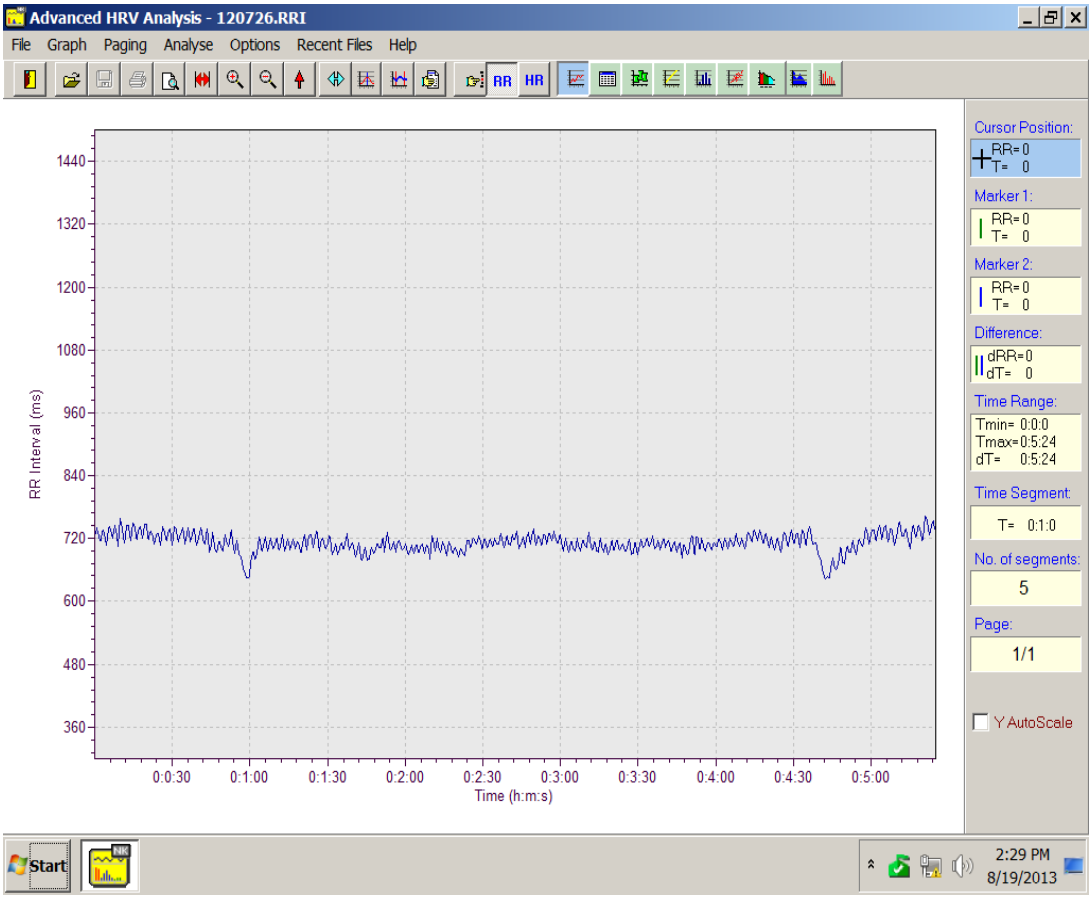

Fig.12. An RR interval tachogram in a cervical cord injury patient with the time interval on the x axis and RR interval duration on the y axis.

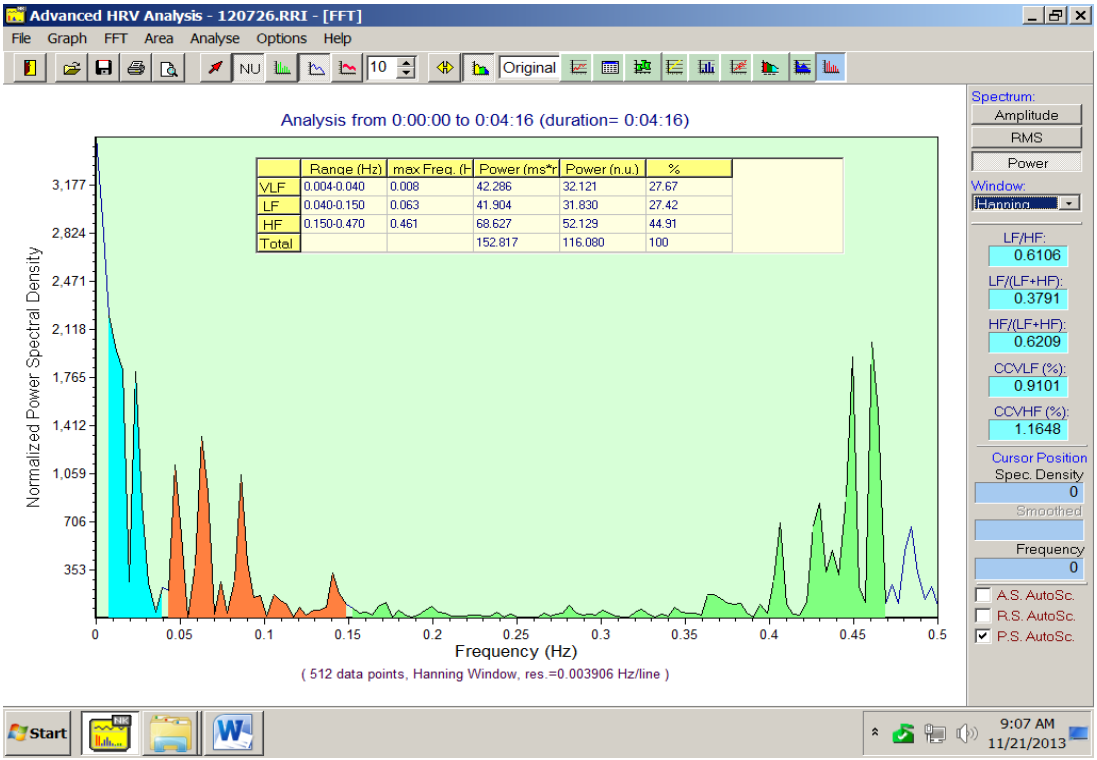

Fig.13. Distribution of power over frequency bands after a power spectral analysis of an RR interval tachogram using Fast Fourier Transform. X axis = Frequency, y axis = Power spectral density.

The frequency domain parameters computed were LF power, HF power, LF/HF ratio, total power (LF+HF), LF power in normalized units and HF power in normalized units.(figure 13) For computing the frequency domain parameters, the software took 256 seconds of data points and applied the Hanning window to prevent the spectral leakage. Power spectral analysis was done using Fast Fourier Transformation (FFT). The power spectral density was obtained by through the Welch's periodogram using the widow width of 512 data points with an overlap of 256 points. Task force guidelines were followed while analysing the HRV. For frequency domain parameters, the frequency range of low-frequency (LF) component was defined as 0.04-0.15Hz and the high-frequency (HF) component as 0.15-0.4Hz (Electrophysiology 1996) The mean respiratory rate in the cervical spinal cord injury

patients was 21.29 ± 2.596 breaths/min. Since respiratory rate affects the HF component, the frequency range of HF component was chosen as 0.15-0.47Hz for the present study.

SSR RECORDING

After 5 minutes of recording the ECG for short term heart rate variability indices, SSR was recorded. The recording system consists of CMCdaq, an amplifier, and an electrode pair. The electrode pair was attached on the subject for recording SSR and further it was amplified by a pre-amplifier of gain 300. The pre-amplifier was designed to operate in 0.05Hz to 300Hz. This filtered, amplified signal was fed to the CMCdaq and was recorded in real-time. The CMCdaq allowed further filtering and gain adjustment via software settings.

After thoroughly scrubbing the skin with cotton soaked in spirit, active electrodes were placed on the palm of the patient's hand (figure14) and reference electrodes were placed on the dorsum of the hand (figure 15) . A ground electrode was placed on the flexor surface of the forearm.

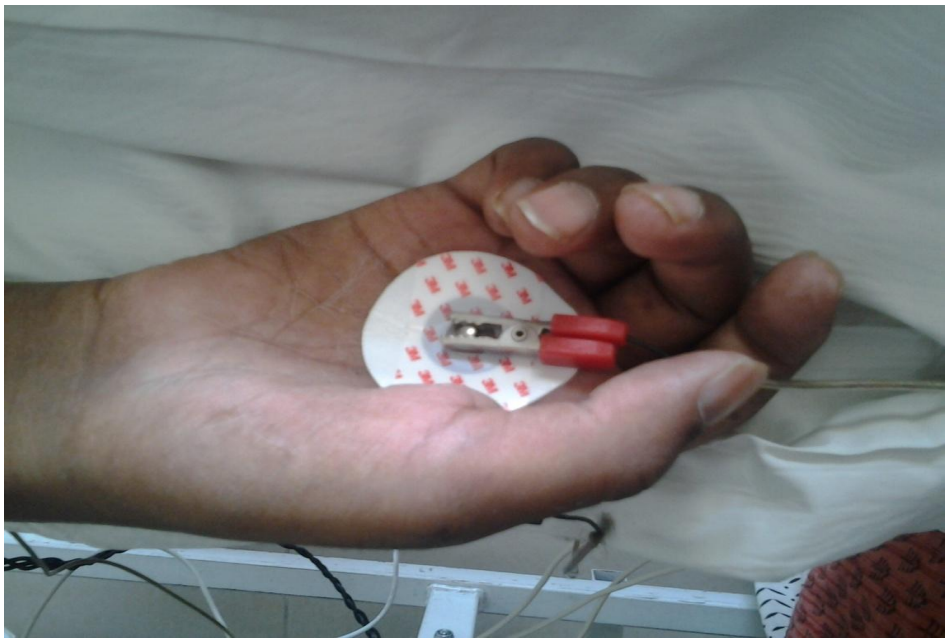

Fig.14. Active electrode placed on the palm of the patient.

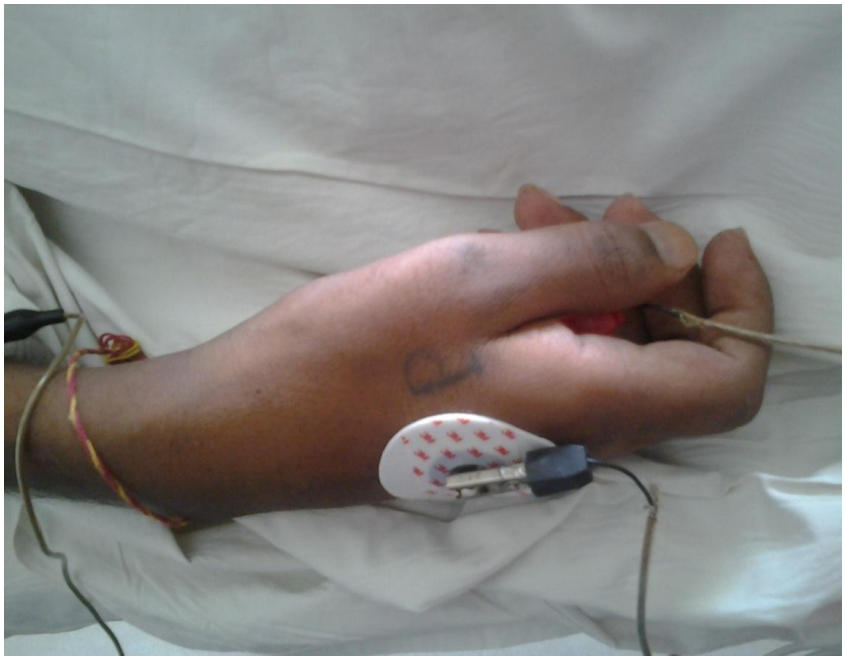

Fig.15. Reference electrode placed on the dorsum of patient's hand.

In the feet, active electrodes were placed on the sole and reference electrodes were placed on the dorsum of the feet (shown in figure 14). Skin temperature was measured before recording the SSR in all patients. The stimulus used to elicit the SSR was a sudden loud blast sound. The rationale was that hearing the sudden loud sound would evoke a sympathetic excitation in the patient leading to sympathetic mediated secretion by the sweat glands and filling of the sweat gland ducts, changing the skin resistance and therefore the potential recorded from the skin.

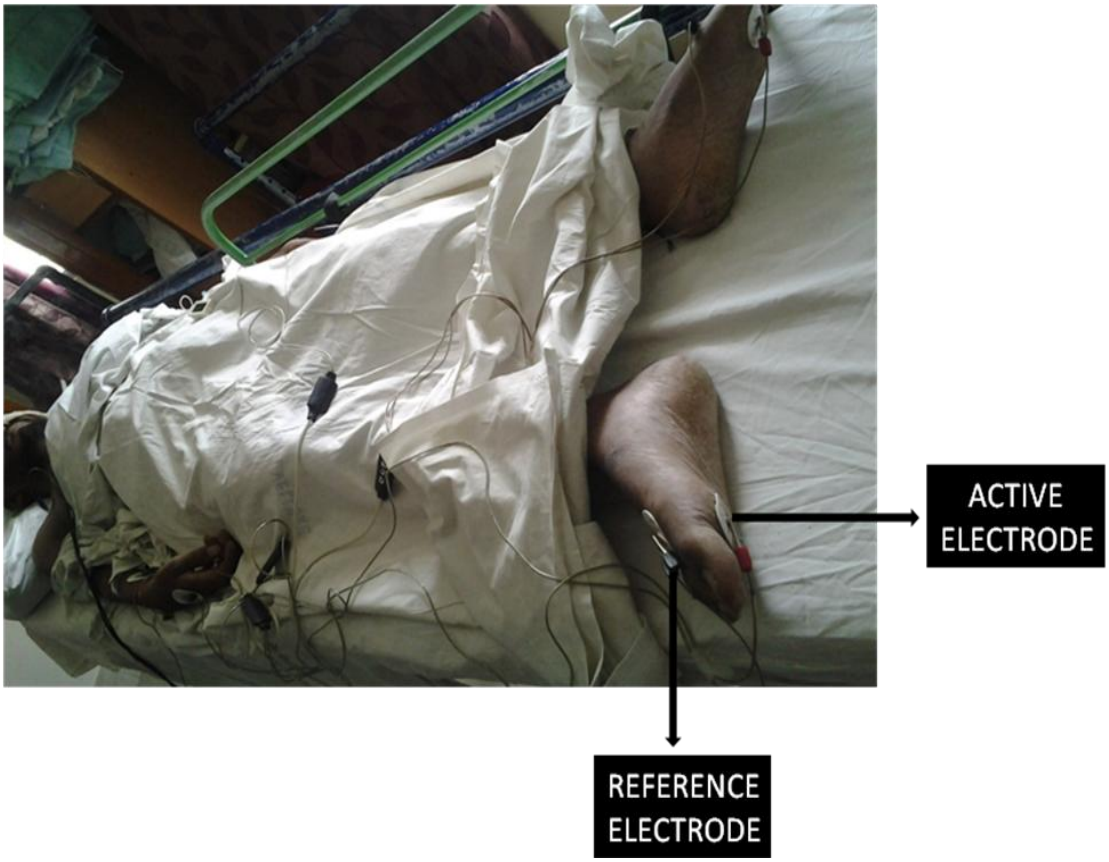

Fig.16. Active and Reference electrodes connected to the sole and dorsum of patient's feet.

A loud blast sound of a gunshot was pre-recorded and saved on the PC. During the experimentation the sound was suddenly played by means of speakers (Creative SBS speaker) connected to the PC, without any prior warning to the patient. To record the digitized auditory signal, the output of the speaker was also bypassed to the CMCdaq (figure 17) using a splitter. The intention was to startle the patient and evoke a sympathetic response. The test was repeated by playing the loud blast sound again at 1 minute interval.

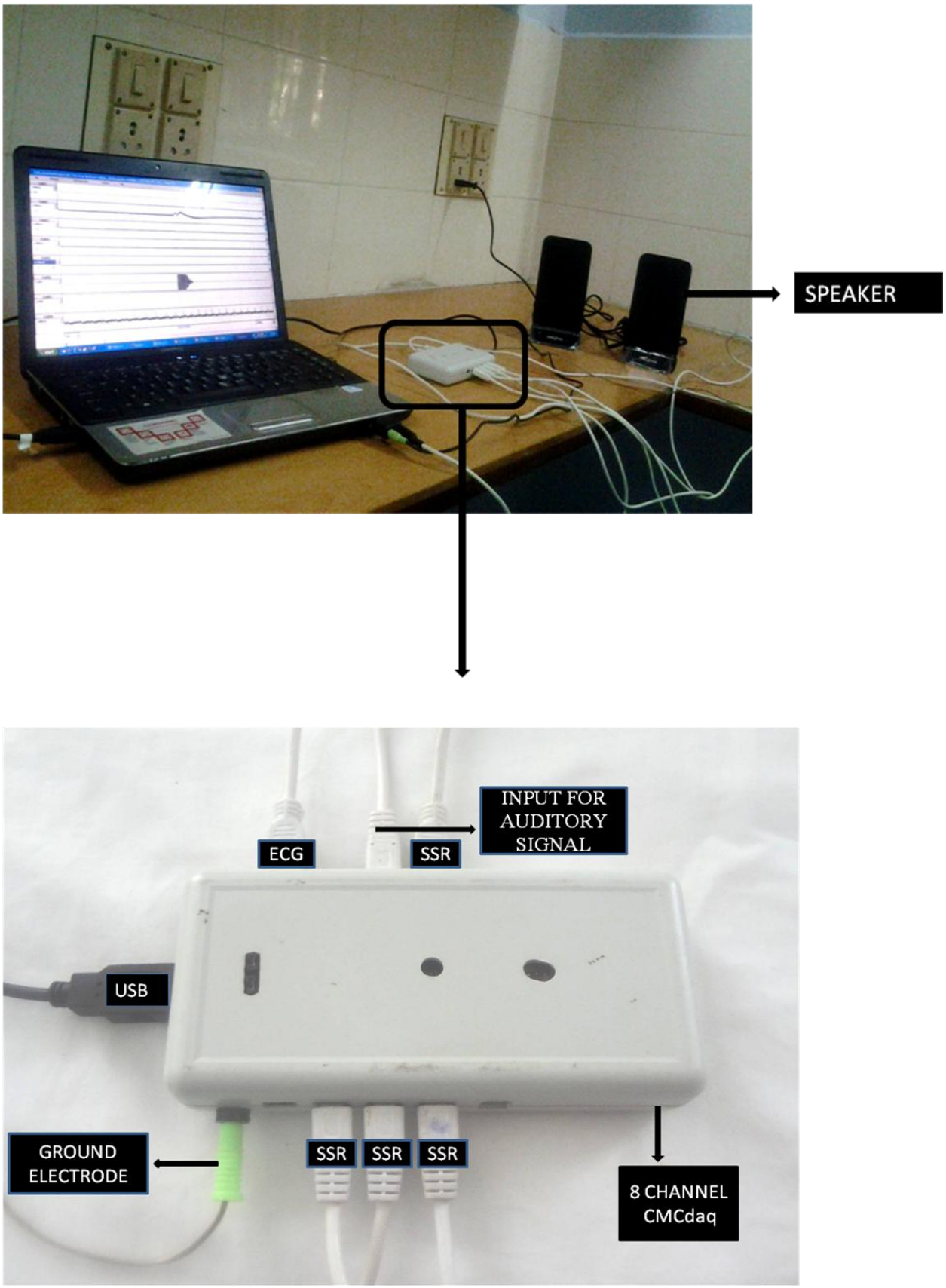

Fig.17. Experimental set up to elicit SSR using auditory stimulus.

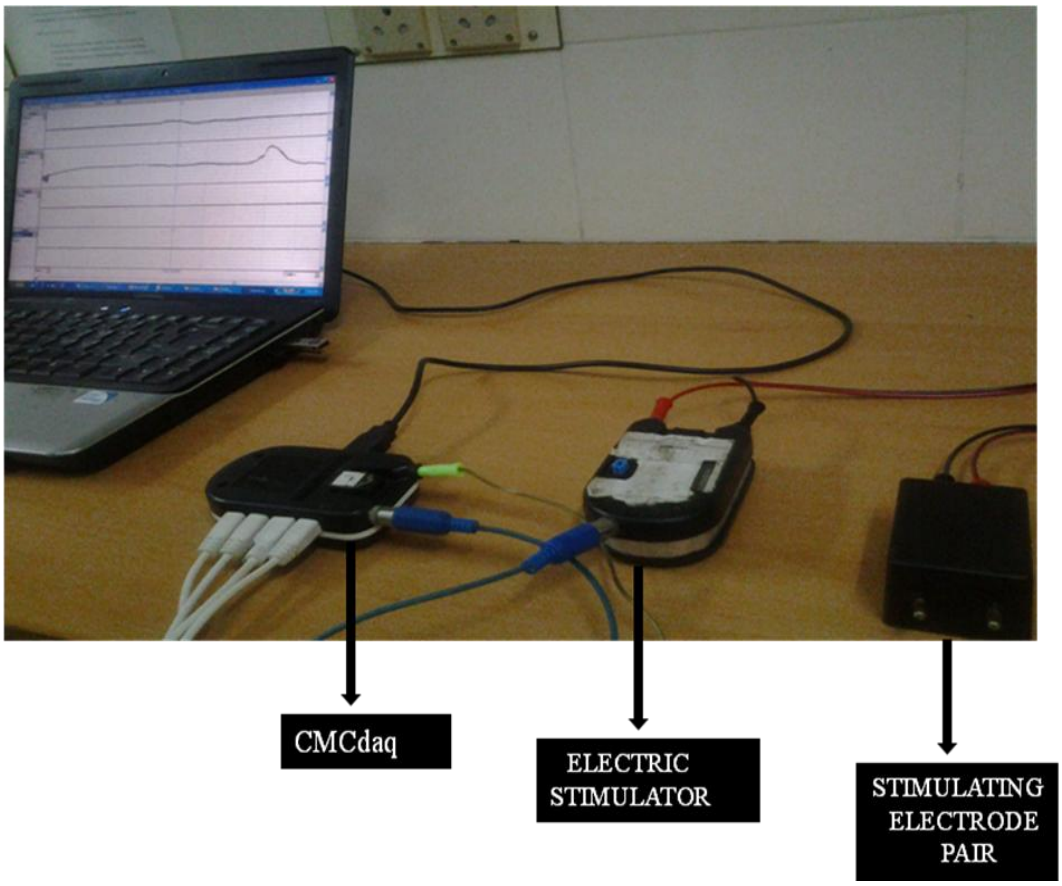

Fig.18. Experimetal setup to elicit SSR using electric stimuli.

If the SSR was not elicited by the audio signal, electrical stimulation of supraorbital nerve was done. For this set up, an electric stimulator (CMCstim), which can be controlled manually using switches, was connected to the 4 channel CMCdaq (figure 18). An electric stimulation of 35 mA, for 0.25 ms duration, was given to the supraorbital nerve of right side using the electric stimulator. (Ogura et al. 2004) The digital signals from the CMCdaq were used to control the CMCstim and the user software had provisions for generating the biphasic pulses, which is shown as an event marker on all the channels to mark the exact time when the stimulation was given. The SSR was recorded simultaneously from all four limbs. If a response was not obtained on any of the 4 limbs, then the stimulation was repeated again at 1

minute interval, before declaring that the SSR was absent. The results of SSR was considered as being either present (+) or absent (-). The patient was considered to have a positive SSR if the SSR was obtained from any one of the 4 limbs. The recording system for SSR was validated on healthy adults prior to every recording. (figure 19 & 20)

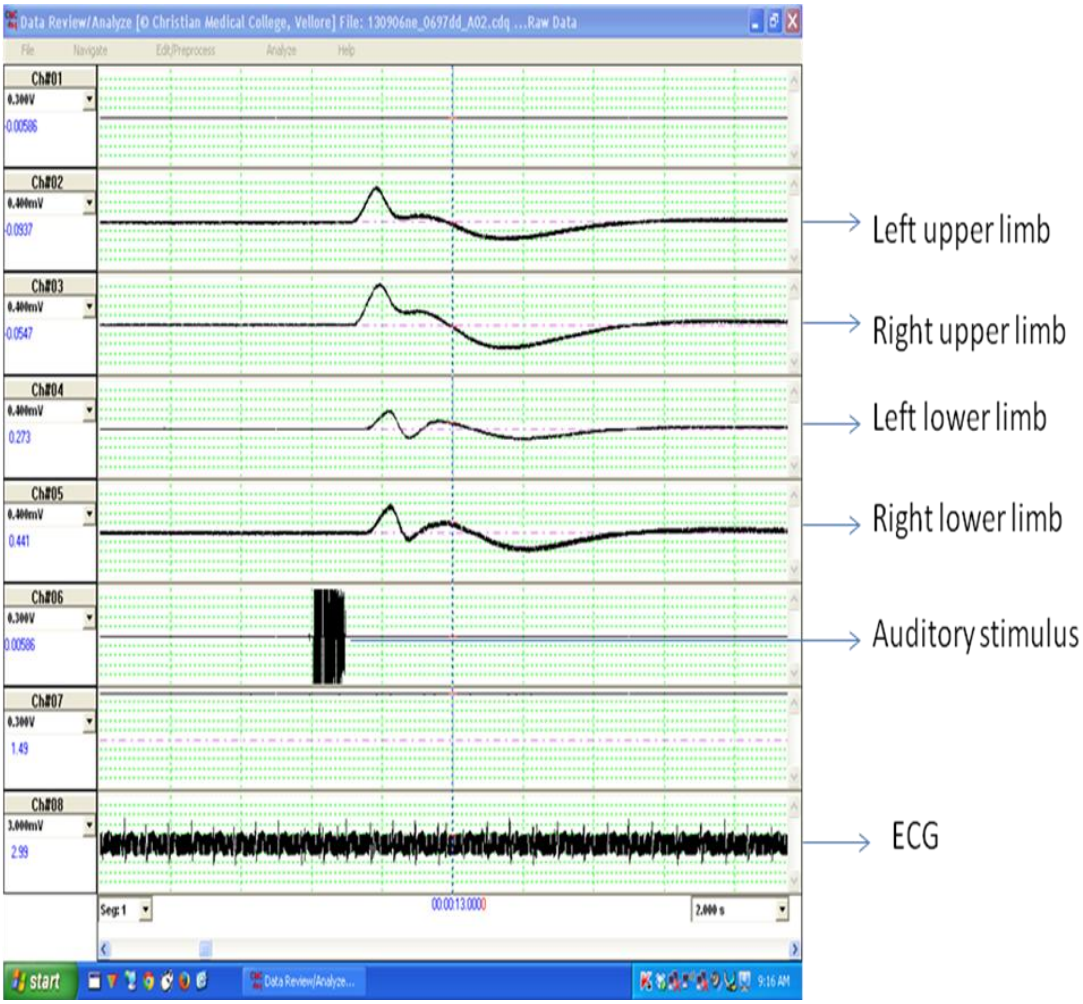

Fig.19. SSR +ve in all four limbs in a healthy subject following an auditory stimulus

SSR was recorded from the 4 limbs simultaneously in four channels. One channel recorded the skin potentials from left upper limb; another channel recorded the skin

potential from right upper limb; still another channel recorded the SSR from left lower limb and yet another channel recorded the SSR from right lower limb; the auditory stimulus was recorded separately on another channel. The ECG which was continuously recorded during the recordings of the SSR was used to note whether sympathetic activation did occur in the patient in response to the auditory stimulus. An increase in heart rate in response to the auditory stimulus was seen in all patients, even those with negative SSR, indicating sympathetic activation.

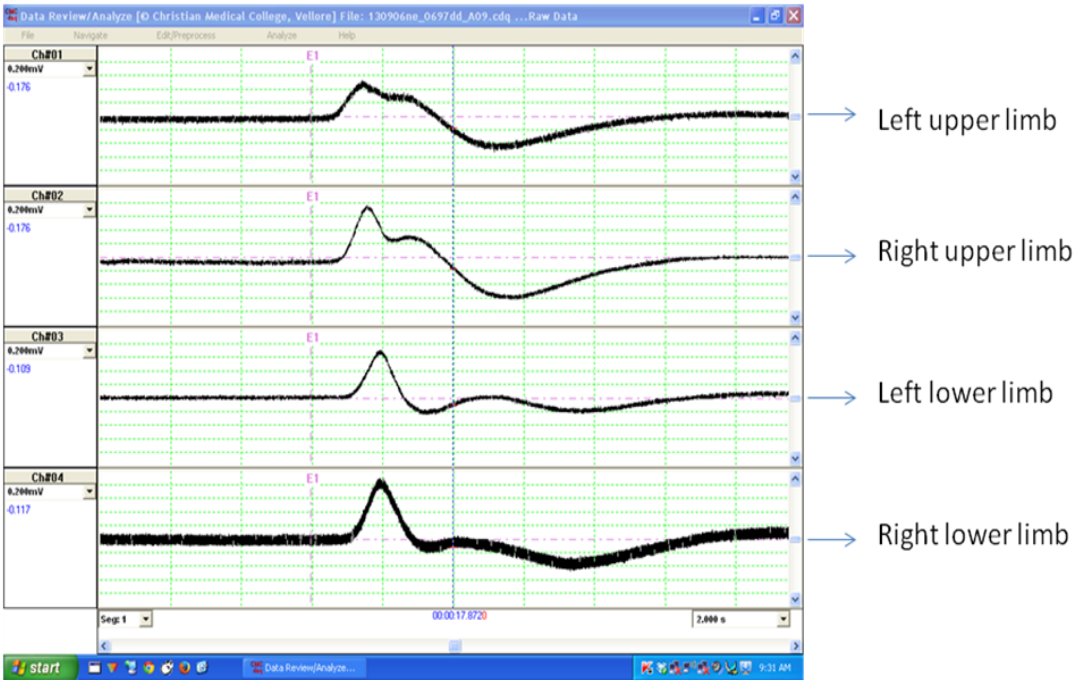

Fig.20. SSR +ve in all four limbs using electric stimuli in a healthy subject. E1 – Event marker denoting exact time point at which the electric stimulus to supra orbital nerve was applied.

STATISTICAL ANALYSIS

The data was not normally distributed. The change in motor and sensory scores were computed and correlated with the HRV indices, using spearman's correlation coefficient.

From the extent of recovery, the patients were categorized into those who had a good recovery (who have shifted from AIS grade A or B to AIS grade C, D or E) and those who had poor recovery (who remain within AIS grade A and B).

Fisher's Exact test was applied to study if there is any association between those patients in whom the SSR was present/absent at the time of admission and those who showed good/poor recovery.

RESULTS

RESULTS

Twenty four (23 male, 1 female) traumatic cervical cord injury patients with age 35.83 ± 14.41 years were recruited into the study. Of them, 11 patients had complete lesion and 13 patients had incomplete lesion. 11 patients were AIS grade A and 13 patients were AIS grade B lesion. The average motor score in the patients was 18.21 ± 12.77 and the average sensory score was 59.46 ± 31.68. The clinical details of the recruited patients are given in table 1.

Table 1. Subjects clinical details.

S.No.	Experiment No.	Age	Sex	SCI level	AIS grade	Lesion	Motor score	Sensory score
1	120726	20	M	C4	A	complete	5	30
2	120905	58	M	C4	B	Incomplete	6	34
3	120913	39	M	C3	A	complete	6	20
4	120928	45	F	C4	A	complete	24	32
5	121201	44	M	C4	B	Incomplete	21	108
6	121206	22	M	C5	A	complete	28	68
7	121207	20	M	C7	A	complete	37	104
8	130109	19	M	C3	A	complete	0	20
9	130110	65	M	C4	B	Incomplete	23	96
10	130215	54	M	C4	B	Incomplete	5	108
11	130222	47	M	C5	B	Incomplete	30	128
12	1302221	15	M	C4	A	complete	0	52
13	130304	25	M	C4	B	Incomplete	4	44
14	130306	24	M	C4	A	complete	4	24
15	130307	44	M	C4	B	Incomplete	34	68
16	130311	38	M	C4	A	complete	6	28
17	130312	48	M	C5	B	complete	28	69
18	130328	27	M	C4	B	Incomplete	28	46
19	130618	26	M	C4	B	Incomplete	10	40
20	130703	19	M	C4	B	Incomplete	19	54
21	130729	54	M	C4	A	complete	28	88
22	130906	26	M	C7	B	Incomplete	41	68
23	130912	42	M	C5	A	complete	28	38
24	130913	39	M	C4	B	Incomplete	22	52

The parameters recorded during the study are resting heart rate, resting respiratory rate, mean arterial pressure, sympathetic skin response and heart rate variability indices. The average mean resting heart rate was 77.276 ± 16.629 beats/min and the Mean RR interval was 811.988 ± 179.154 ms. The average resting respiratory rate was 21.29±2.596 breaths/min. The parameters recorded during the study are shown in table 2 & 3.

Table 2. Parameters recorded during the study.

S.No.	Resting Heart Rate	Mean Arterial Pressure	Resting Respiratory Rate	Skin tempe-rature	SSR Present/absent
1	84.56	83.33	24	29.6	+
2	63.92	93.33	15	32	+
3	97.68	80.00	20	32	-
4	56.00	70.00	24	30	-
5	104.75	70.00	22	28.7	-
6	68.17	70.00	18	29	-
7	73.49	70.00	28	30.8	-
8	63.72	83.33	24	32	-
9	84.61	98.00	20	27	-
10	66.53	93.33	21	30	-
11	69.90	90.00	20	29	-
12	69.78	86.67	18	28	-
13	81.26	90.00	20	32.6	+
14	64.25	86.67	21	32.2	+
15	67.42	96.67	20	31.5	+
16	107.81	83.33	20	32	+
17	77.02	93.33	21	31.3	+
18	45.27	83.33	24	32.2	-
19	66.37	96.67	21	33.2	+
20	99.75	83.33	22	32.7	+
21	88.14	96.67	22	31.2	+
22	65.75	93.33	23	27.3	-
23	82.98	96.67	23	30.1	-
24	105.50	83.33	20	30.5	-

SHORT TERM HEART RATE VARIABILITY INDICES

TIME DOMAIN PARAMETERS

The average SDNN in the patients was 35.93 ± 30.73 ms and RMSSD was 33.75 ± 34.54 ms. The average pNN50 was 13.66 ± 17.21 %.

Table 3. Mean RR interval and Time domain parameters. (n = 24)

S.No.	Mean RR interval(ms)	SDNN(ms)	RMSSD(ms)	pNN50(%)
1	709.55	17.64	16.57	0.00
2	938.69	37.10	29.54	7.81
3	614.25	31.57	8.90	0.00
4	1071.46	45.19	59.72	48.21
5	572.8	14.69	8.69	0.00
6	880.09	58.81	33.94	12.02
7	816.42	20.92	18.41	0.69
8	941.56	73.28	86.63	58.31
9	709.14	51.85	16.37	2.12
10	901.89	15.64	10.10	0.00
11	858.36	35.54	41.87	28.00
12	859.85	37.09	42.60	28.95
13	738.34	19.83	26.35	1.23
14	933.79	71.47	50.39	31.99
15	889.89	32.78	33.96	12.78
16	556.53	5.27	4.12	0.00
17	779.04	24.07	33.59	12.69
18	1325.4	150.45	166.77	39.47
19	904.02	33.23	40.46	23.80
20	601.51	7.47	4.52	0.00
21	680.74	21.26	25.06	3.89
22	912.61	34.47	34.81	15.73
23	723.07	15.84	8.11	0.00
24	568.7	6.78	8.48	0.17
MEAN	811.99	35.93	33.75	13.66
STDEV	179.15	30.73	34.54	17.21

All values are expressed as mean ± standard deviation. SDNN - Standard deviation of the normal to normal RR intervals, RMSSD - Root mean square of successive differences between adjacent RR intervals, pNN50 - percentage of number of RR intervals with differences > 50ms.

FREQUENCY DOMAIN PARAMETERS

The average LF power in the patients was 546.94 ± 1344.32 ms^2. HF power was found to be 535.13 ± 1084.76 ms^2. Total power was 1082.07 ± 2421.87 ms^2. LF/HF ratio was 1.05 ± 1.00. LF nu (normalised units) was 0.43± 0.19 nu and HF nu was 0.57 ± 0.19 nu.

Table 4. Frequency domain parameters. (n= 24).

S.No.	LFpower (ms^2)	HFpower (ms^2)	LF+HFpower (ms^2)	LF/HF ratio	LF nu	HF nu
1	41.90	43.48	85.38	0.96	0.49	0.51
2	224.87	557.37	782.24	0.40	0.29	0.71
3	106.59	23.98	130.57	4.44	0.82	0.18
4	1054.70	726.74	1781.44	1.45	0.59	0.41
5	7.27	28.35	35.63	0.26	0.20	0.80
6	683.04	372.87	1055.90	1.83	0.65	0.35
7	149.71	61.13	210.84	2.45	0.71	0.29
8	1400.67	1330.18	2730.85	1.05	0.51	0.49
9	118.58	86.74	205.32	1.37	0.58	0.42
10	32.44	34.08	66.52	0.95	0.49	0.51
11	232.02	634.91	866.93	0.37	0.27	0.73
12	232.02	634.91	866.93	0.37	0.27	0.73
13	21.63	206.72	228.35	0.10	0.09	0.91
14	1058.21	1008.74	2066.95	1.05	0.51	0.49
15	216.54	341.16	557.70	0.63	0.39	0.61
16	1.82	6.06	7.87	0.30	0.23	0.77
17	61.69	179.79	241.48	0.34	0.26	0.74
18	6597.63	5343.49	11941.12	1.23	0.55	0.45
19	385.68	580.92	966.60	0.66	0.40	0.60
20	6.38	11.08	17.45	0.58	0.37	0.63
21	71.74	96.30	168.05	0.74	0.43	0.57
22	373.35	508.41	881.76	0.73	0.42	0.58
23	46.56	16.26	62.82	2.86	0.74	0.26
24	1.43	9.47	10.90	0.15	0.13	0.87
MEAN	546.94	535.13	1082.07	1.05	0.43	0.57
STDEV	1344.32	1084.76	2421.87	1.00	0.19	0.19

All values are expressed as mean ± standard deviation. LF – Low Frequency, HF – High Frequency, nu – normalized units.

MOTOR AND SENSORY SCORE

Motor and sensory score was assessed again at the time of discharge and the AIS grades revised accordingly.

Table 5. Motor and sensory score assessed at the time of admission and at the time of discharge. (n=24)

S.No.	Experiment No.	Admission motor score	Discharge motor score	Admission sensory score	Discharge sensory score
1	120726	5	15	30	30
2	120905	6	7	34	64
3	120913	6	14	20	32
4	120928	24	34	32	100
5	121201	21	23	108	112
6	121206	28	38	68	127
7	121207	37	40	104	128
8	130109	0	2	20	34
9	130110	23	38	96	98
10	130215	5	6	108	124
11	130222	30	36	128	108
12	1302221	0	6	52	50
13	130304	4	41	44	122
14	130306	4	6	24	31
15	130307	34	57	76	100
16	130311	6	8	28	32
17	130312	28	32	69	144
18	130328	28	28	46	100
19	130618	10	20	40	32
20	130703	19	26	54	60
21	130729	28	28	88	96
22	130906	41	48	68	99
23	130912	28	18	38	40
24	130913	22	23	52	48

CHANGE IN MOTOR AND SENSORY SCORE

The change in motor and sensory score at the time of discharge compared to that at the time of admission were computed. The sum of change in the motor and sensory score in the patients were given in the table 6.

Table 6. Change in motor score and sensory score in cervical cord injury patients. (n=24)

S.No.	Experiment No.	Change in motor score	Change in sensory score	Sum of change in motor and sensory score
1	120726	10	0	10
2	120905	1	30	31
3	120913	8	12	20
4	120928	10	68	78
5	121201	2	4	6
6	121206	10	59	69
7	121207	3	24	27
8	130109	2	14	16
9	130110	15	2	17
10	130215	1	16	17
11	130222	6	-20	-14
12	1302221	6	-2	4
13	130304	37	78	115
14	130306	2	7	9
15	130307	23	24	47
16	130311	2	4	6
17	130312	4	75	79
18	130328	0	54	54
19	130618	10	-8	2
20	130703	7	6	13
21	130729	0	8	8
22	130906	7	31	38
23	130912	-10	2	-8
24	130913	1	-4	-3

CORRELATION BETWEEN HRV INDICES AND THE CHANGE IN MOTOR AND SENSORY SCORE

Correlation between HRV indices and the change in motor score (table 8), change in sensory score (table 9) and the sum of change in the motor and sensory score (table 10) were done using spearman's correlation coefficient.

Table 7. Correlation between mean RR interval and the change in motor score, change in sensory score and the sum of change in motor and sensory score. (n=24)

	Mean RR interval	Significance (p value)
Correlation coefficient with change in motor score	0.004	0.984
Correlation coefficient with change in sensory score	0.430	0.036
Correlation coefficient with sum of change in motor and sensory score	0.399	0.053

Table 8. Correlation between HRV indices and change in motor score. (n=24)

HRV indices	Correlation coefficient with change in motor score	Significance (p value)
SDNN	0.150	0.485
RMSSD	0.146	0.497
PNN50	0.101	0.639
LF	0.094	0.661
HF	0.110	0.610
LF+HF	0.173	0.418
LF/HF	0.000	1.000
LF nu	0.000	1.000
HF nu	0.000	1.000

Table 9. Correlation between HRV indices and change in sensory score. (n=24)

HRV indices	Correlation coefficient with change in sensory score	Significance (p value)
SDNN	0.275	0.194
RMSSD	0.285	0.177
PNN50	0.222	0.297
LF	0.246	0.246
HF	0.270	0.202
LF+HF	0.366	0.078
LF/HF	0.157	0.465
LF nu	0.157	0.465
HF nu	0.157	0.465

Table 10. Correlation between HRV indices and sum of change in motor and sensory score. (n=24)

HRV indices	Correlation coefficient with change in score	Significance (p value)
SDNN	0.333	0.112
RMSSD	0.292	0.166
PNN50	0.215	0.312
LF	0.252	0.234
HF	0.270	0.202
LF+HF	0.373	0.073
LF/HF	0.184	0.390
LF nu	0.184	0.390
HF nu	-0.184	0.390

RESULTS OF SSR

The patient was classified as SSR positive, even if the SSR was elicited in only one of the four limbs. The patient was classified as SSR negative, only if SSR was absent in all four limbs. In this study, the amplitude and latency of SSR was not considered. Just the presence or absence of SSR was considered to classify the patients into those who were SSR positive and SSR negative.

SSR USING AUDITORY STIMULI

Figures 21 & 22 shows SSR elicited in patients in response to loud blast sound.

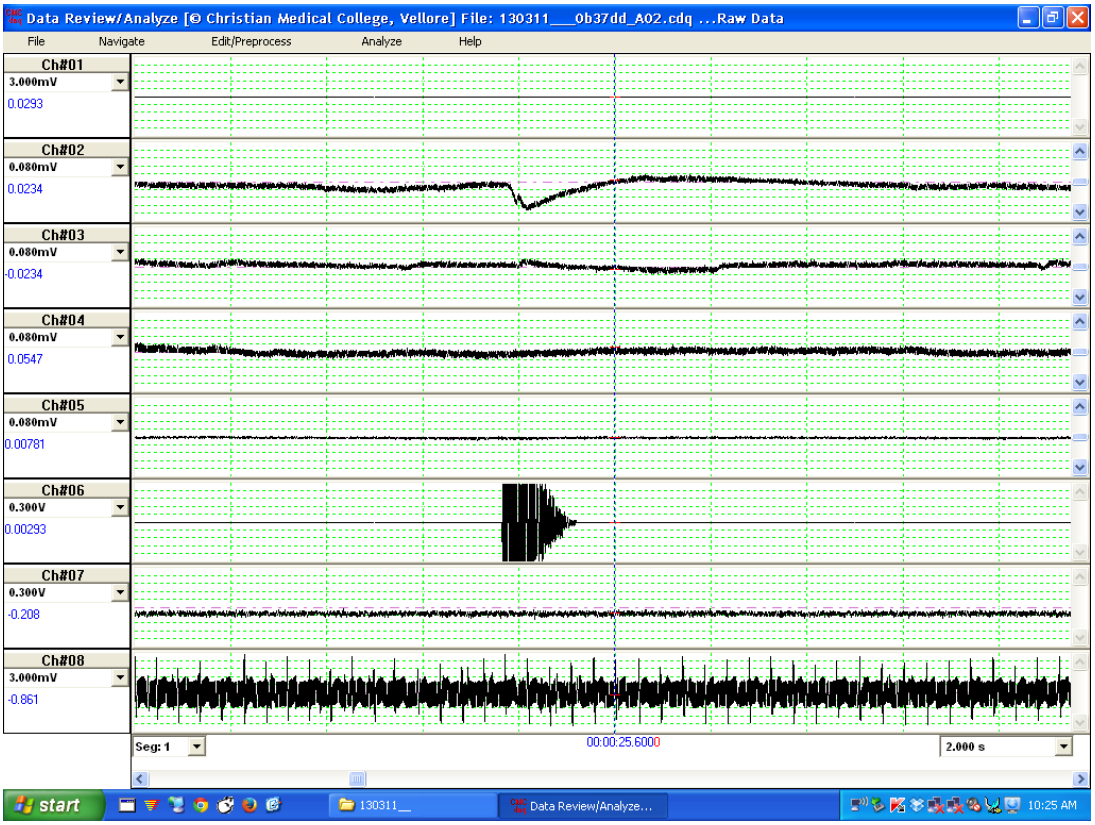

Fig.21. SSR positive in the first channel (Left Upper limb) in a cervical cord injury patient using blast sound. (This patient was SSR positive)

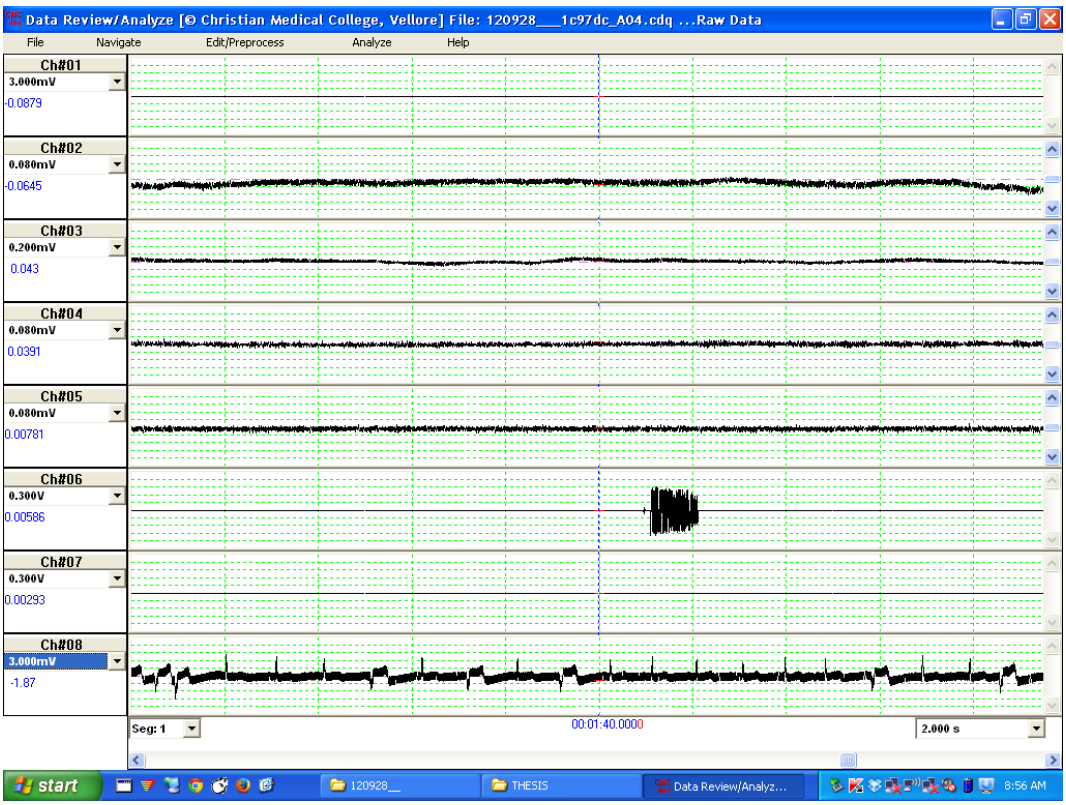

Fig.22. The skin potentials did not change in response to a blast sound in this cervical level SCI patient. (This patient was SSR negative)

In this figure, SSR is –ve in all four limbs

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SSR USING ELECTRIC STIMULI

Figure 23 & 24 shows the SSR elicited in patients in response to electrical stimuli

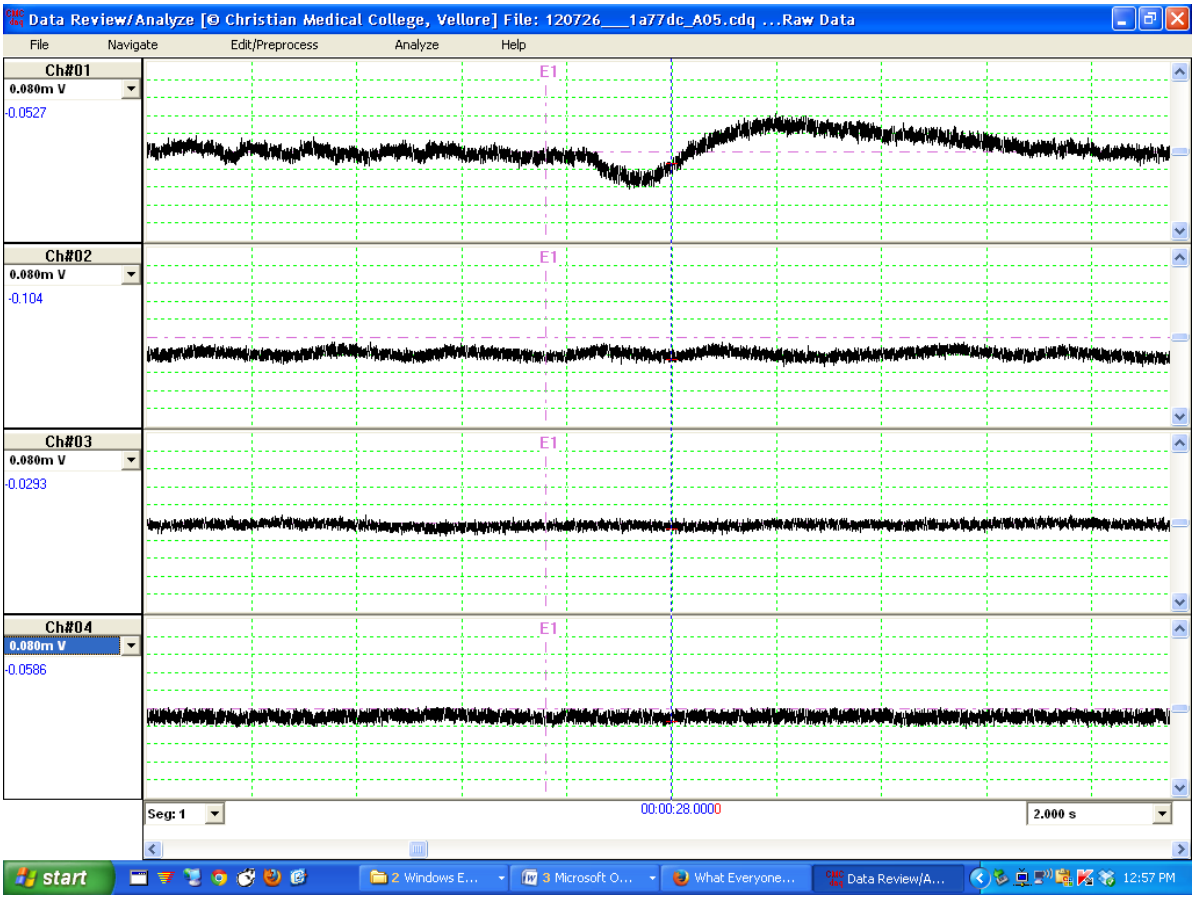

Fig.23. SSR positive in the first channel (Left Upper limb) recorded in a cervical cord injury patient by electric stimuli. E1 – Event marker for electric stimuli. (This patient was SSR positive)

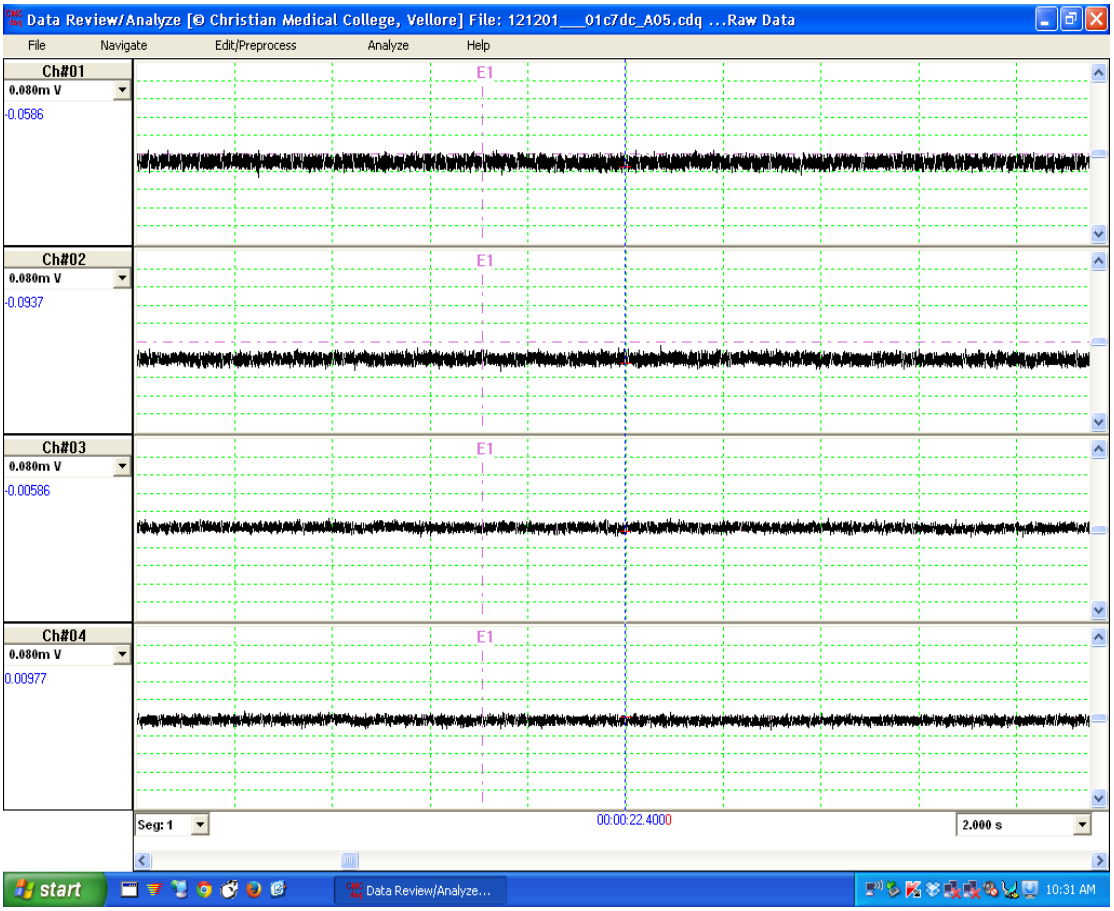

Fig.24. The skin potentials did not change in response electric stimuli in this cervical SCI patient. E1- Event marker for electric stimuli. (This patient was SSR negative)

In this figure, SSR is –ve in all four limbs.

IMPROVEMENT IN AIS GRADE

If the patients shifted from AIS grades A and B recorded at the time of admission, to AIS grades C, D or E at the time of discharge, they were categorized under good recovery. If the patient continues to remains within AIS grade A and B at the time of discharge or shift from AIS A at the time of admission to AIS B at the time of discharge, they were categorized under poor recovery. Table 11 gives the AIS grades and SSR of the patients.

Table 11. Improvement in AIS grade and SSR of patients.

S.No.	AIS grade at time of admission	AIS grade at time of discharge	Improvement in AIS Grade	SSR
1	A	A	Poor	+
2	B	B	Poor	+
3	A	A	Poor	-
4	A	B	Poor	-
5	B	B	Poor	-
6	A	C	Good	-
7	A	A	Poor	-
8	A	A	Poor	-
9	B	C	Good	-
10	B	B	Poor	-
11	B	B	Poor	-
12	A	A	Poor	-
13	B	C	Good	+
14	A	A	Poor	+
15	B	C	Good	+
16	A	A	Poor	+
17	B	C	Good	+
18	B	B	Poor	-
19	B	A	Poor	+
20	B	A	Poor	+
21	A	A	Poor	+
22	B	B	Poor	-
23	A	A	Poor	-
24	B	A	Poor	-

ASSOCIATION BETWEEN SSR AND IMPROVEMENT IN AIS GRADE

Association between SSR and improvement in AIS grade in the patients is shown below.

Table 12. Association between SSR and improvement in AIS grade.(n=24)

SSR	Improvement in AIS grade		Total
	Good	Poor	
Positive (+ve)	3	7	10
Negative (–ve)	2	12	14
Total	5	19	24

Out of 24 patients, 3 patients with SSR + ve showed good improvement.

7 patients with SSR + ve showed poor improvement.

2 patients with SSR – ve showed good improvement.

12 patients with SSR – ve showed poor improvement.

By applying Fisher's Exact test, there was no statistically significant association between SSR and improvement in AIS grade. (p value = 0.615)

DISCUSSION

DISCUSSION

The present study investigated whether there was any relationshiip between the cardiac autonomic status of traumatic cervical SCI patients at the time admission and their subsequent recovery. Similarly, another objective of the study was to explore if there was any association between SSR at the time of admission and subsequent clinical improvement of the cervical cord injury patients.

The intention of these objectives was to see if measurements of cardiac autonomic status and sympathetic skin response would help in prognostication of patients. The descending autonomic fibres which supply the cardiac autonomic spinal output and the sudomotor supply to the sympathetic sweat glands may or may not be intact in a traumatic cervical SCI patient.

It was hypothesised that those patients with greater HRV indices and positive SSR would have intact descending autonomic pathway and hence chance of some motor and sensory fibres to be intact and therefore greater recovery would be expected in them. Similarly, those patients with lower HRV indices and negative SSR would have complete lesion of both the autonomic and the motor and sensory pathways and therefore poorer recovery would be expected in them. There are very few studies which have investigated the integrity of the autonomic pathways in the spinal cord injury patients. And there are no studies correlating the autonomic findings of SCI patients with clinical recovery of the patients.

Currently, the patients are classified at the time of injury merely by the motor and sensory findings which reflect the integrity of the motor and sensory pathways without taking into account the integrity of the autonomic pathways. It was postulated that investigating the integrity of the autonomic pathway may provide additional

information in classifying the patients at the time of admission and further help in predicting the functional improvement of the patients.

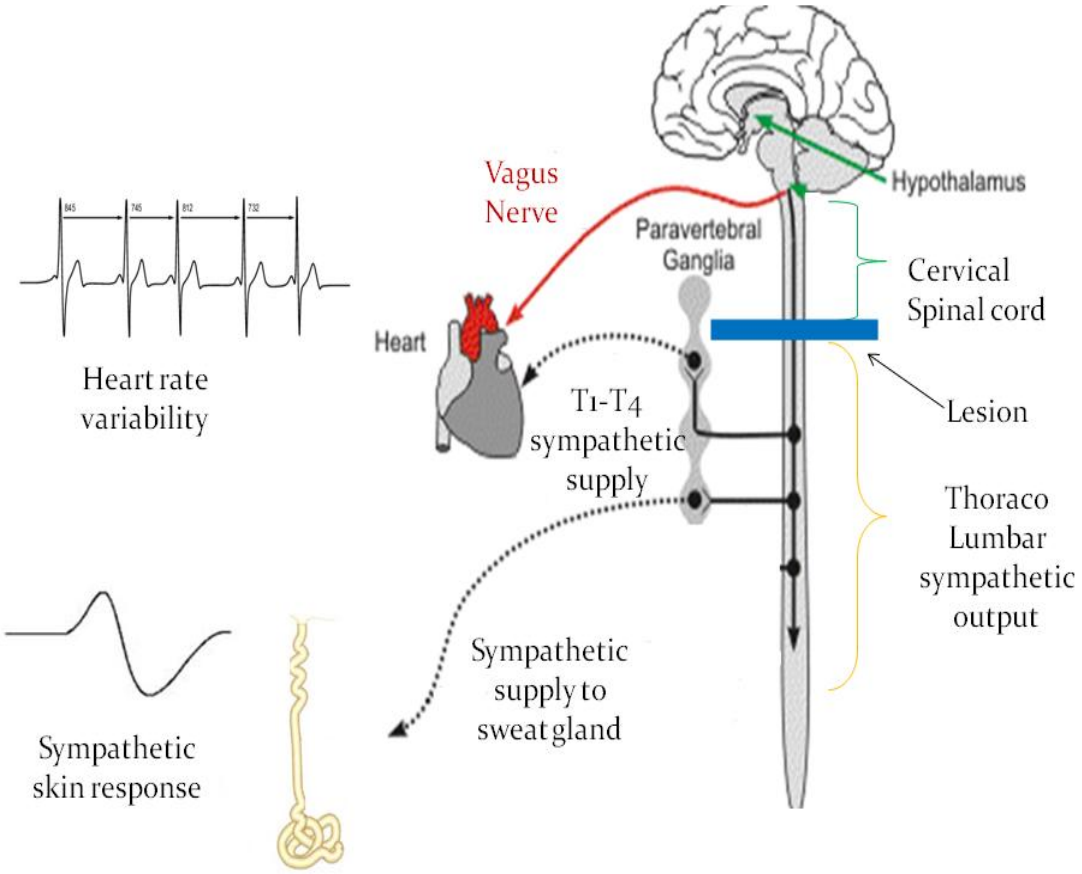

Fig.25. Autonomic pathways in cervical spinal cord injury (lesion above T1).

In the present study, the short-term heart rate variability indices and sympathetic skin response in twenty four traumatic cervical SCI patients were studied and their relationship with motor and sensory recovery and AIS grade were analysed. All twenty four SCI patients were AIS grade A or B at the time of admission. The most common level of lesion was C4. These were the patients who were admitted under the

department of Physical Medicine and Rehabilitation. Parameters assessed at the time of admission were resting heart rate, resting respiratory rate, mean arterial pressure, SSR and short-term HRV indices.

SCI patients with lesions such as tumours, syringomyelia, cervical spondylosis and tuberculsis were excluded from the study as damage caused by these pathological conditions are progressive. Trauma on the other hand occurs at one point in time and its basic pathophysiology is not progressive. There is only scope for clinical improvement of the traumatic SCI patients with therapy. Which patients would improve with therapy and to what extent, is the difficult question that the treating physician is faced with at the time of admission of the patients. Often the patients relatives decide on the extent of time and resources to be kept aside for treatment of the patient depending on the prognosis of the patient or the predicted recovery of the patient.

The findings of the present study indicate that studying the cardiac autonomic status of quadriplegic traumatic cervical SCI patients, through short-term HRV analysis and SSR are not helpful in predicting the functional recovery of the patients.

Discussion of each of the findings are given below.

HRV

The SA node which is the pacemaker of the heart is supplied by the parasympathetic and sympathetic nervous system. Modulations of the sympathetic and parasympathetic cardiac supply modulate the firing rate of the SA node and is responsible for the beat-to-beat variation of the RR interval in milliseconds,which is known as the HRV.The control of the sympathetic supply to the heart from the higher

centres is expected to be lost in cervical SCI patients. Hence, the HRV would also get altered in these patients. (Claydon& Krassioukov 2008) (Grimm et al. 1997) Since the inputs from the higher centres to the spinalsympathetic centres contribute to the fluctuations in the spinal sympathetic output to the heart, patients with severed autonomic descending pathways would be expected to have less modulation of the RR intervals by sympathetic nervous system and therefore lower HRV. Moreover, a decrease in modulation of the cardiac parasymapthetic supply also occurs in SCI patients as a compensatory mechansim to maintain sympatho-vagal balance. (Grimm et al. 1997) Patients with intact descending autonomic control of sympathetic fibres would thus be expected to have higher HRV.

The LF power, an output of the Frequency domain analysis of HRV mainly reflects the cardiac sympathetic activity. (Electrophysiology 1996) Some studies report a marked decrease in the LF power in quadriplegic SCI patients, with only HF power contributing to the total power. (Inoue et al. 1995) This would be due to the lack of modulation of the cardiac sympathetic supply. In yet another study the finding was that when the LF power reduced there was a corresponding decrease in the HF power of the quadriplegic SCI patients. The authors postulate that this occurred as a homeostatic mechanism to maintain sympatho-vagal balance. (Grimm et al. 1997)

The mean resting heart rate of the patients was 77.28 ± 16.63 beats per min. This was a much higher value than expected. In a patient with lesion of spinal cord, the heart rate is expected to be lower due to disruption of the descending sympathetic pathways. The high heart rate seen in these patients may be due to vagal withdrawal unmasking the intrinsic firing rate of the SA node which is 100-110 bpm. The vagal centre in the medulla supplying the heart is still under the control of the higher autonomic centre in the hypothalamus. As HRV was analysed soon after the injury,at

a time when the SCI patients are under considerable mental and emotional stress, the limbic inputs to the hypothalamic centres would have contributed to increase in heart rate. The hypothalamic outputs to the cardiac vagal centre would have been inhibitory producing the vagal withdrawal and an increase in heart rate or a decrease in the mean RR interval. Moreover baroreceptor inputs would have a role in inhibiting the vagal supply to the heart.

It is worth mentioning that the mean RR interval showed a weak correlation with the change in sensory score (spearman's correlation coefficient r is 0.430, P value = 0.036). This implies that the patients with higher RR interval (or lower heart rate) showed higher improvement in sensory score. This finding may be interpreted to understand that patients with less baseline stress and therefore lower resting heart rate are inclined to have greater improvement in sensory score. It may also be interpreted to understand that those patients who did not improve had greater stress and therefore higher heart rate. However, it must be kept in mind that the mean RR interval is not a heart rate variability index. Mean RR interval reflects the sympatho-vagal balance on the firing rate of the SA node.

The average change in the motor score in the patients was 6.54 ± 9.03 and the average change in sensory score was 20.27 ± 27.39. Similar to the present study, in a study by Waters et al, the average increase in the motor score between one month and one year was found to be 8.6 ± 4.7 and the rate of motor recovery declined during first 6 months and attained plateau.(Waters et al. 1993)

The study showed no correlation between heart rate variability indices and the improvement in the motor and sensory scores considered separately and as a sum.

Thus in the present study analysis of the HRV indices in traumatic quadriplegic SCI patients was not helpful in predicting recovery.

SSR

The sudomotor fibres supplying the sweat glands originate from the thoracolumbar spinal sympathetic centres, which receive descending input from higher control centres. The SSR was used in the present study to assess the integrity of these descending autonomic fibres to the spinal sympathetic centres. The SSR is the recording of the change in the skin potential that occurs due to secretion of sweat by the sweat glands in response to sympathetic stimulation. In the quadriplegic patients, supraspinal stimuli was used to produce excitation of the thoracolumbar sympathetic sudomotor output. The stimuli consisted of an auditory stimulus in the form of a sudden loud sound and electric stimulation of the suprorbital nerve, both of which would startle the patient and trigger a hypothalamic mediated sympathetic response. Sweat gland secretion and the related change in skin potential would occur in response to these supraspinal stimuli only if the descending autonomic fibres from the hypothalamus to the spinal sympathetic centres is intact. The findings of the present study revealed that SSR occurred in 10 of the 24 quadriplegic patients.

An important objective of the present study was to explore whether there was any association between the presence (or absence) of SSR in the quadriplegic patients at the time of admission and their subsequent recovery. For this purpose, we classified patients who shifted from AIS grade A/B to grade C/D/E at the end of the rehabilitation programme as those showing 'Good' recovery, while those patients who continued to remain in AIS grade A/B was classified as those showing 'Poor' recovery. 4 AIS B patients shifted to AIS C at the end of rehabilitation and 1 AIS A

patient shifted to AIS C at the end of rehabilitation. The findings of the present study is similar to a previous study where 3.6% of AIS A patients shifted to AIS C at the time of discharge and 36.8% of AIS B patients shifted to AIS C at the time of discharge.(Marino 2007) Fisher's exact test was then used to study the association between the 2 categorical variables, one being the presence or absence of SSR and the other being 'Good' or 'Poor' recovery. The results of this statistical analysis revealed that there was no association between the outcome of the SSR at the time of admission and the eventual clinical improvement of the patients. Thus 3 (30%) of the patients who had a positive SSR had a good recovery while 7 (70%) of the patients with positive SSR had poor recovery. 2 (14%) of the patients who had a negative SSR had a good recovery while 12 (86%) of the patients with negative SSR had poor recovery.

Various factors can affect SSR like high dose of anticholinergic drugs and habituation. In the present study, patients who were on anticholinergic drugs and other drugs which affects the autonomic nervous system were taken off the drugs for four days prior to the examination under physician's supervision. This increased the reliability of the results of the SSR test in the present study.

Habituation to repeated stimulation has been reported as a phenomenon which can affect the results of the SSR test. (Aramaki et al. 1997) To avoid habituation when repetitive stimulation is applied, care should be taken to ensure that the there should be atleast 1 min between two stimulus. (Nagarajarao et al. 2006) In the present study, both the auditory and electric stimuli were given at 1 minute interval. And between auditory and electric stimuli, 5 min interval was given. Further, in some patients, SSR was negative with auditory stimuli which was given first and SSR was positive with the electric stimuli which was given after the auditory stimuli. This clearly shows that

habituation was not seen in them while eliciting the SSR. Published literature reports that SSR can be reverted back if the stimulation for SSR is altered from electric to magnetic stimuli. (Toyokura 2006)

Ambient temperature is also known to affect the outcome of the SSR test, especially the SSR latency and amplitude. (Kucera et al 2004) In the present study all the recordings of SSR was done at a room temperature of around 25°C. The skin temperature of the patients was also noted prior to eliciting the SSR. The average skin temperature was 30.6 ±1.76°C and the skin temprature ranged from 27°C to 33.2°C in all the 24 patients. Low skin temperature decreases the amplitude and increases the latency of sympathetic skin response. (Deltombe et al)

SSR can be evaluated qualitatively and quantitatively. Some authors prefer qualitative evaluation i.e. considering only the absence of SSR as a pathological sign. (Soliven et al. 1987) Other group of authors prefer quantitative evaluation i.e. latency parameters (Karataş et al. 2002) and amplitude parameters. Clinically, it is useful to practice qualitative evaluation i.e. absence of SSR. (Kucera et al. 2004) In the present study, presence or absence of SSR was considered for reporting the results of the SSR test.

In a study by Cariga et al, SSR was –ve in all complete cervical spinal cord injury patients (AIS A). SSR was absent in AIS B cervical cord injury patients where they could feel the activating stimuli. (Cariga et al. 2002) In contrast to their findings, in the present study, SSR was positive in 5 of the AIS grade A as well as in 5 of the AIS grade B patients. In the present study, SSR was considered positive if the amplitude of the skin potential changed (negative or positive) by more than 0.2 mV. The amplitude of the SSR in all patients was found to be less than 0.5 mV.

In a study by Nagarajarao et al, SSR was positive in the hands in 2 out of 6 patients with AIS A cervical cord injury and SSR was positive in 1 out of 4 patients with AIS B,C and D. This finding shows that SSR can be elicited in a complete spinal cord injury patient (Nagarajarao et al. 2006) and supports the findings of the present study. The results imply that the descending autonomic pathways to the spinal sympathetic centres were intact in these patients even though they had varying degrees of lesion of the motor and sensory tracts.

In the present study, 2 AIS grade A/B patients with absent SSR (SSR –ve) at the time of admission showed good functional recovery at the time of discharge. And 7 patients with positive SSR at the time of admission showed poor recovery. There was no statistically significant association between SSR results and recovery outcome. Thus clearly there was no evidence from the findings of the present study to conclude that SSR test results would help to predict the recovery pattern of the patients. Categorizing AIS grade A/B patients into those with positive SSR and negative SSR was not useful to prognosticate in this study.

The study did not reveal any statistically significant association between the presence or absence of SSR at the time of admission with the improvement in AIS grade at the end of the rehabilitation programme.

LIMITATION

LIMITATION

The present study expored the resting cardiac and sudomotor activity. Autonomic function tests by provocative methods such as cold pressor test, response to isometric exercise and headup tilt tests were not investigated. Whether there is a relationship between these test results and the clinical recovery of patients were not studied.

CONCLUSION

CONCLUSION

In the present study, short-term HRV indices and SSR were not found to be useful parameters to prognosticate recovery in traumatic cervical cord injury AIS grade A/B quadriplegic patients. Assessment of the integrity of the descending autonomic pathways provided no additional useful information towards classifying these patients at the onset of the illness, in the current study.

FUTURE COURSE

FUTURE COURSE

The autonomic response to provocative studies such as the Cold pressor test, Head-up tilt test and response to isometric exercise could be studied in cervical SCI patients and looked for correlation with clinical recovery.

SUMMARY

SUMMARY

Spinal cord injury leads to neurological deficit. Some patients with cervical cord injury recover well. While other patients do not show any signs of improvement. There is a need to assess which patients may recover when the patients are admitted for rehabilitation therapy, as this is a question uppermost in the minds of not only the treating doctor but also the patients themselves and their relatives. So far there is no proven way to assess the prognosis of the traumatic cervical SCI patients. Currently examination of the motor and sensory systems of the patients is used to categorize them. Patients with less severe motor and sensory score and in AIS grade C and D are expected to recover better. However recovery of the AIS grade A and B patients is unpredictable. Would assessment of the integrity of the descending autonomic pathways, through evaluation of the cardiac autonomic status and SSR of AIS grade A/B patients, provide more information to help classify patients at the start of therapy? The present study was designed to address this question and to fill the gap in assessing the prognosis of the patients at the earliest.

So far, there are no studies relating cardiac autonomic control and intactness of the descending autonomic fibres, with motor and sensory recovery in SCI patients. Therefore, there was a need to study the autonomic functions in relation with recovery in SCI patients.

We hypothesised that those cervical SCI patients with higher HRV indices and positive SSR may have intact descending autonomic pathway and may also have chance for some intact motor and sensory pathways and therefore they may have good recovery. On the other hand, those patients with lower HRV indices and negative SSR may not have intact autonomic and motor and sensory pathways and

hence they may have poor recovery. Hence, by assessing the integrity of the descending autonomic tract through SSR and HRV, at the time of admission, it may be possible to identify the cervical SCI patients who may show good motor and sensory recovery.

Traumatic cervical cord injury quadriplegic patients in AIS grade A or B were recruited into the study after informed consent. At the time of admission, once the patients were hemodynamically stable, the autonomic integrity was assessed through HRV and SSR.

The short-term HRV indices obtained at the time of admission were studied for correlation with the change in motor and sensory scores at the time of discharge of the patients, with the aim of studying whether higher values of HRV indices would be able to predict a greater improvement in motor and sensory scores. The findings of sympathetic skin response were studied for association with poor and good recovery of the patients in terms of AIS grade.

The present study did not show any statistically significant correlation between the HRV indices and the change in motor and sensory scores. Neither was there any statistically significant association between the presence or absence of SSR at the time of admission and the subsequent improvement in AIS grade.

In the present study short-term HRV indices and SSR were not found to be useful parameters to prognosticate the recovery in traumatic cervical cord injury quadriplegic patients in AIS grade A/B.

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ANNEXURES

ANNEXURE I

Table 1. Subjects clinical details.

S.No.	EXP. DATA	HOSPITAL ID	AGE	SEX	CAUSE OF INJURY	SMOKER
1	120726	233106F	20	M	RTA	YES
2	120905	284592F	58	M	RTA	YES
3	120913	282286F	39	M	FFH	YES
4	120928	295353F	45	F	RTA	NO
5	121201	328909F	44	M	RTA	YES
6	121206	359154F	22	M	FFH	NO
7	121207	352710F	20	M	RTA	YES
8	130109	350557F	19	M	RTA	NO
9	130110	367403F	65	M	RTA	NO
10	130215	389432F	54	M	FFH	YES
11	130222	396620F	47	M	RTA	NO
12	130222 1	374073F	15	M	RTA	NO
13	130304	402378F	25	M	RTA	YES
14	130306	339528F	24	M	RTA	NO
15	130307	406916F	44	M	RTA	NO
16	130311	381544F	38	M	FFH	NO
17	130312	401222F	48	M	RTA	NO
18	130328	421391F	27	M	FFH	YES
19	130618	486853F	26	M	LOAD	YES
20	130703	600984F	19	M	RTA	NO
21	130729	620896F	54	M	FFH	NO
22	130906	643367F	26	M	RTA	NO
23	130912	611468F	42	M	RTA	YES
24	130913	628408F	39	M	RTA	YES

RTA- Road Traffic Accident, FFH- Fall From Height, LOAD- Load on neck.

ANNEXURE – II

Patient Information sheet

Study Title: ***Study of relationship between initial autonomic functions and subsequent motor and sensory recovery in traumatic cervical cord injury patients***

You are being requested to participate in a study which aims to compare the nervous control of heart and sweat glands at the time of admission and the subsequent improvement in muscle strength (muscles of arms and leg) and touch and pain sensation, at the time of discharge.

If you take part what will you have to do and what will happen to you?

If you agree to participate in this study, your ECG and respiration will be recorded for about 20 minutes. This will be done by applying ECG electrodes and a belt around your chest, making sure that you are comfortable and relaxed, in a quiet room. This recording will assess the nervous control of your heart. Electrodes to record voltage produced by sweat glands of the skin will be applied to both the hands and feet. Then you will be made to hear a loud sound to activate the sweat glands. If the loud sound does not activate the sweat glands then a small electric current will be applied for a few milliseconds, to the nerve of your forehead to activate the sweat glands. In this way we will be able to assess the nervous control of the sweat glands of your hands and feet.

The muscle strength and the pain and touch sensation of your arms and legs will be assessed both at the time of admission and at the time of discharge, to study the extent of improvement.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are free to decide to withdraw from this study at any time.

What will happen if you develop any study related injury?

We do not expect any injury to happen to you.

Will you have to pay for the tests?

The testing is free.

Will your personal details be kept confidential?

The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, the data collected from you may be reviewed by people associated with the study, without your additional permission.

If you have any further questions, please contact:

1) Dr.LATHA(CMCextn:4268/Cell:9965614312) or email: latha2011@cmcvellore.ac.in

2) Dr. ABHISHEK SANYAL (cell: 9791731348/ CMC extn: 4549)

3) Dr. ROHIT BHIDE (cell: 9791322090/ CMC extn: 2158)

CONSENT FORM

Study Title:

Study of relationship between initial autonomic functions and subsequent motor and sensory recovery in traumatic cervical cord injury patients

---

Participant's name:

Date of Birth / Age (in years):

I_____

_____, son/daughter of _____

(Please tick boxes)

I declare that I have read /been read to the information sheet provided to me regarding this study and I have clarified any doubts that I had. [ ]

I also understand that my participation in this study is entirely voluntary and that I am free to withdraw at any time. [ ]

I understand that the study staff and institutional ethics committee members will not need my permission to look at my data, even if I withdraw from the study. I agree to this access. [ ]

I understand that my identity will not be revealed in any information released to third parties or published. [ ]

I voluntarily agree to take part in this study [ ]

Name:

Signature/Thumb impression:

Date:

Name of witness:

Signature:

Date:

கிருத்துவமருத்துவக்கல்லூரி

தகவல்படிவம்

ஆராட்சியின்தலைப்பு:

கழுத்தின்தண்டுவடத்தில்காயம்ஏற்பட்டவர்களுக்குஆரம்பத்துலுள்ளஇருதயமற்றும்வியர்வைசுரப்பிகளின்நரம்புமண்டலத்திற்கும்,
பயிற்சிகாலம்முடிந்தபின்புதசைமற்றும்உணர்ச்சிகள்எந்தஅளவுமுன்னேற்றம்அடையும்என்பதற்கும்தொடர்புஉண்டாஎன்பதைபற்றியஆராட்சி

1.நீங்கள்இவ்வாராட்சியில்பங்குகொள்கிறீர்கள்என்றால்,நீங்கள்செய்யவேண்டியவைமற்றும்நீங்கள்உங்களுக்குசெய்யப்படுபவை:

நீங்கள்இவ்வாராட்சியில்பங்குகொள்கிறீர்கள்என்றால்,உங்களதுசுருள்படம்மற்றும்சுவாசம்இருபது நிமிடங்கள்பதிவுசெய்யப்படும்.இவைஒருஅமைதியானஇடத்திலசெய்யப்படும்.நீங்கள்தளர்த்தப்பட்டுஇருக்கவேண்டும்.உங்கள்மார்பைச்சுற்றிஒருபெல்ட்டும்,சுருள்படத்திற்க்கானஎமின்முனைகளும் பொருத்தப்படும்.இந்தபதிவுமூலம்இருதயநரம்புகட்டுப்பாடுமதிப்பிடமுடியும்.உங்கள்இருகைகள்மற்றும்இருகால்களில்உள்ளதோலின்வியர்வைசுரபிகளின்நரம்பியல்செயல்பாட்டைக்கண்டறிய, ஒருசப்தமானஒலிகொடுக்கப்படும். இம்முறையில்கண்டறியமுடியவில்லைஎன்றால், சிறியமின்சாரமஒருசிலமில்லிவினாடிகளுக்குஉங்கள்நெற்றியிலுள்ளநரம்புஒன்றில்செயல்படுத்தப்படும்.வியர்வைசுரபியின்நரம்புநிலையைக்கண்டறியஎலக்ட்ரோடுகளைஉங்கள்இருகைகள்மற்றும்கால்களில்பொருத்தப்படும்.

2.இந்தஆராய்ச்சியில்தாங்கள்பின்வாங்கமுடியுமா?

தாங்கள்ஆராய்ச்சியில்பங்கேற்பதுதங்களின்சொந்தமுடிவுஆகையால்,
தாங்கள்எப்பொழுதுவேண்டுமானாலும்பின்வாங்கலாம்.

3.இந்தஆராட்சியின்மூலம்ஏதேனும்உடல்சார்ந்தகேடுஏற்படுமா?

இந்தஆராட்சியில்எந்தகேடும்ஏற்படாது.

4.இச்சோதனைகளுக்கு, ஏதேனும்கட்டணம்வசூலிக்கப்படுமா?

இச்சோதனை, முற்றிலும்இலவசமானது.

5. தாங்கள்ஆள்சார்தகவல்கள்ரகசியமாகவைக்கப்படுமா?

இந்தஆராய்ச்சியிலிருந்துவரும்விவரங்கள்,மருத்துவபத்திரிக்கைகளில்வெளியிடப்படும்.ஆனாலும்உங்களதுமருத்துவவிவரங்கள்இந்தஆராய்ச்சியில்பங்குபெறும்ஆராய்சியாளர்கள்மட்டும்காணமுடியும்.இவர்கள்இத்தகவல்களைஉங்களதுகூடுதல்அனுமதியின்றிகாணலாம்.

உங்களுக்குஏதேனும்சந்தேகம்இருந்தால்கீழ்க்கண்டடாக்டர்களைதொடர்புகொள்ளலாம்:

1 .மரு.லதாதொலைபேசி எண்:9965614312,மின் அஞ்சல்:latha2011@cmcvellore.ac.in

2. மரு. அபிஷேக்சன்யல் தொ.எண்.9791731348எண்.4549

3. மரு .ரோஹித்பிட் தொ.எண்.9791322090எண். 2158

கிருத்துவமருத்துவக்கல்லூரி, வேலூர் .

ஒப்புதல்படிவம்

ஆராட்சியின்தலைப்பு :
கழுத்தின்தண்டுவடத்தில்காயம்ஏற்பட்டவர்களுக்குஆரம்பத்துலுள்ளஇருதயமற்றும்வியர்வைசுரப்பிகளின்நரம்புமண்டலத்திற்கும்,
பயிற்சிகாலம்முடிந்தபின்புதசைமற்றும்உணர்ச்சிகள்எந்தஅளவுமுன்னேற்றம்அடையும்என்பதற்கும்தொடர்புஉண்டாஎன்பதைபற்றியஆராட்சி .

பங்குபெறுவோரின்பெயர் :
பிறந்ததேதி :
வயது :
நான் .....த/பெ.....

[ ] இடங்களில்குறியிடவும்
1 . எனக்குகொடுத்ததகவல்படிவத்தைபடித்து / படிக்கக்கேட்டு புரிந்துகொண்டேன் [ ]
2 .
நான்இந்தஆராட்சியில்பங்குகொள்வதுஎனதுசொந்தமுடிவுஎன்றும்,இதிலிருந்துஎப்பொழுதுவேண்டுமானாலும்விலகிகொள்ளலாம்என்றும்அறிவேன் [ ].

3 .என்னுடையஆள்சார்தகவல்களைநான்ஆராய்ச்சியிலிருந்துவிலகிக்கொண்டாலும், என்னுடையகூடுதல்அனுமதியின்றிஆராய்ச்சியாளர்கள்எப்பொழுதுவேண்டுமானாலும்பார்க்கலாம்என்றும்நான்அறிவேன் [ ].

4 .என்னுடையஆள்சார்தகவல்கள்வெளியிடப்படாதுஎன்றுநான்அறிவேன்[ ].

5 . இந்தஆராய்ச்சியில்நான்பங்குகொள்வது, என்னுடைய சொந்தமுடிவாகும் [ ].

பெயர் :

கையெப்பம்/பெருவிரல்அடையாளம் :

தேதி :

சாட்சிபெயர் :

கையெப்பம்:

தேதி :

सहमति फार्म

अध्ययन शीर्षक :

प्रारंभिक स्वास्थ्य कार्य और बाद में मोटर और दर्दनाक ग्रीवा की हड्डी में चोट के रोगियों में संवेदी वसूली के बीच संबंधों का अध्ययन।

1. भागीदार का नाम :
2. जन्म की तिथि / आयु (वर्षों में)

मैं , का

पुत्र / पुत्री,

(कृपया बकसे टिक करें)

1. मैं घोषणा करता हूँ कि इस अध्ययन के बारे में मुझे प्रदान, पत्र मैंने पढ़ा है और मुझे कोई संदेह नहीं है, सब कुछ स्पष्ट है।
2. मैं समझता हूँ कि इस अध्ययन में मेरी भागेदारी पूरी तरह स्वैच्छित है और मैं किसी भी समय वापसी ले सकता हूँ।
3. मैं समझता हूँ कि अध्ययन कर्मचारियों और संस्थागत नैतिकता समिति के सदस्यों को मेरी अनुमति नहीं चाहिए, मेरे डेटा को परखने के लिए, यहाँ तक कि, वे मेरा डेटा, मेरे अध्ययन से निकलने के बाद भी देख सकते हैं। उन्हे यह अधिकार है।
4. मैं समझता हूँ कि मेरी पहचान किसी तीसरे पक्ष को जारी नहीं की जाएगी या प्रकाशित जानकारी मे खुलासा नहीं किया जाएगा।
5. मैं स्वेच्छा से इस अध्ययन में भाग लेने की अनुमति देता हूँ।

- नाम :
- हस्ताक्षर / अंगूठे का निशान :
- दिनांक :

साक्षी का नाम :
हस्ताक्षर :
दिनांक

क्रिस्टियन मेडिकल कॉलेज

मरीज़ जानकारी पत्र

अध्ययन शीर्षक : प्रारंभिक स्वास्थ्य कार्य और बाद में मोटर और दर्दनाक ग्रीका की हड्डी में चोट के रोगियों में संवेदी वसूली के बीच में संबंध का अध्ययन |

आपको इस पत्र के द्वारा एक अध्ययन में भाग लेना और हिस्सा लेने का अनुरोध किया जा रहा है ; जो प्रवेश के समय दिल और पसीने की ग्रंथियों की तंत्रिकाओं की तुलना, और बाद में मांसपेशियों (हाथों और पैरों की मांसपेशियों) की शक्ति और स्पर्श और दर्द में सुधार को आँचता है।

1. यदि आप भाग लेते हैं तो आपको क्या करना होगा और क्या किया जाएगा
- यदि आप इस अध्ययन में भाग लेते है, तो आपका ईसीजी और श्वास कृया 20 मिनट तक दर्ज की जाएगी। यह आपके सीने के आसपास इलेक्ट्रोड और एक बैल्ट लगाकर किया जाएगा। आप आरामदायक और एक शांत कमरे में होंगे। यहाँ दिल की तंत्रिका नियंत्रण रिकॉर्डिंग का आलंकन करेंगे। त्वचा की पसीने की ग्रंथियों द्वारा निर्मित वोलटेज, रिकॉर्ड करने के लिए इलैक्ट्रोड़ दोनो हाथों और पैरों मे लगाए जाएँगे।

फिर पसीने की ग्रंथियोंको सक्रिय करने के लिए, आपको एक ऊँची आवाज़ सुनाई जाएगी।

अगर आवाज पसीने की ग्रंथियों को सक्रिय नहीं करती तो कुछ क्षणों के लिए, धीमा सा विधुत प्रवाह, आपके माथे की तंत्रिका में लगा दिया जाएगा। इस प्रकार हम आपके हाथों और पैरों के पसीने की ग्रंथियों की तंत्रिका नियंत्रण का आकलन करेंगे।

आपके हाथों और पैरों की मासपेशियों की ताकत, दर्द और स्पर्श सनसनी, प्रवेश और छुट्टी, दोनों बार मूल्यांकित की जाएँगी।

1. क्या अध्ययन शुरू होने के बाद आप इससे वापसी ले सकते हैं?
- इस अध्ययन में आपकी भागेदारी पूरी तरह स्वैच्छिक है। आप किसी भ समय, वापसी लेने का फैसला करने के लिए स्वतंत्र हैं।

2. क्या होगा अगर किसी भी प्रकार अध्ययन संबंधित चोट का विकास हो?
- आपको कोई चोट आए, ऐसी कोई आशंका नहीं है।

3. क्या आपको परीक्षण के लिए भुगतान करना होगा?
- यह एक मुफ्त परीक्षण है।

4. क्या आपकी व्यक्तिगत जानकारी गोपनीय रखी जाएगी।
- इस अध्ययन के परिणामों को एक मेडिकल जर्नल में प्रकाशित किया जाएगा, लेकिन आप किसी परिणाम के प्रकाशन या प्रस्तुति में नाम से नहीं पहचाने जाएंगे।
हालांकि, आप से एकत्र आंकड़ों के अध्ययन के साथ जुड़े लोगों द्वारा समीक्षा की जा सकती है।
किसी और प्रश्न के उत्तर के लिए, कृपया संपर्क करें:

1. Dr. Latha (tel: CMC extn. 4268 / cell: 9965614312) or email: latha2011@cmcvellore.ac.in.
2. Dr. Abhishek Sanyal (cell: 9791731348 / extn.: 4549)
3. Dr. Rohit Bhide (cell: 9791322090 / extn. 2158)

ANNEXURE III

INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE
VELLORE 632 002, INDIA

Dr.B.J.Prashantham, M.A.,M.A.,Dr.Min(Clinical)
Director, Christian Counseling Centre
Editor, Indian Journal of Psychological Counseling
Chairperson, Ethics Committee, IRB

Dr. Alfred Job Daniel, MS Ortho
Chairperson, Research Committee &
Principal

Dr. Nihal Thomas
MD, MNAMS, DNB(Endo), FRACP(Endo), FRCP(Edin)
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

March 17, 2012

Dr. Latha N
PG Demonstrator
Department of Physiology
Christian Medical College
Vellore 632 002

Sub: **External Research grant project NEW PROPOSAL :(Department of Science and Technology)**
Study of the relationship between initial autonomic functions and subsequent motor and sensory recovery, in traumatic cervical spinal cord injury patients.
Dr. Latha N, PG Demonstrator, Physiology, Dr. Renu Elizabeth Tharion, Professor, Physiology, Dr. Abhishek Sanyal, PMR, Dr. Bhide Rohit Prakash, PMR, Dr. Grace Rebekah Samuel, Senior demonstrator, Biostatistics

Ref: IRB Min. No. 7694 dated 12.12.2011

Dear Dr. Latha,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "Study of the relationship between initial autonomic functions and subsequent motor and sensory recovery, in traumatic cervical spinal cord injury patients" on December 12, 2011.

The Committees reviewed the following documents:

1. Format for application to IRB submission
2. Patient Information Sheet and Informed Consent Form (English and Tamil)
3. A CD containing documents 1 - 2

TEL : 0416 - 2284294, 2284202 FAX : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE
VELLORE 632 002, INDIA

Dr.B.J.Prashantham, M.A.,M.A.,Dr.Min(Clinical)
Director, Christian Counseling Centre
Editor, Indian Journal of Psychological Counseling
Chairperson, Ethics Committee, IRB

Dr. Alfred Job Daniel, MS Ortho
Chairperson, Research Committee &
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MD, MNAMS, DNB(Endo), FRACP(Endo), FRCP(Edin)
Secretary, Ethics Committee, IRB
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The following Institutional Review Board (Ethics Committee) members were present at the meeting held on December 12, 2011 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore- 632002.

Name	Qualification	Designation	Other Affiliations
Dr. B.J.Prashantham	MA (Counseling), MA (Theology), Dr Min(Clinical)	Chairperson(IRB)& Director, Christian Counselling Centre	Non-CMC
Mr. Harikrishnan	BL	Lawyer	Non-CMC
Mrs. S. Pattabiraman	BSc, DSSA	Social Worker, Vellore	Non-CMC
Mrs. Ellen Ebenezer Benjamin (on behalf of Dr. Jayarani Premkumar)	M.Sc. (Nursing), Ph.D.	Nursing Superintendent, CMC.	
Dr. Gagandeep Kang	MD, PhD, FRCPath.	Secretary IRB (EC)& Dy. Chairperson (IRB), Professor of Microbiology & Addl. Vice Principal (Research), CMC.	

We approve the project to be conducted as presented.

The Institutional Review Board expects to be informed about the progress annually of the project, any serious adverse events occurring in the course of the project, any changes in the protocol and the patient information/informed consent and requires a copy of the final report.

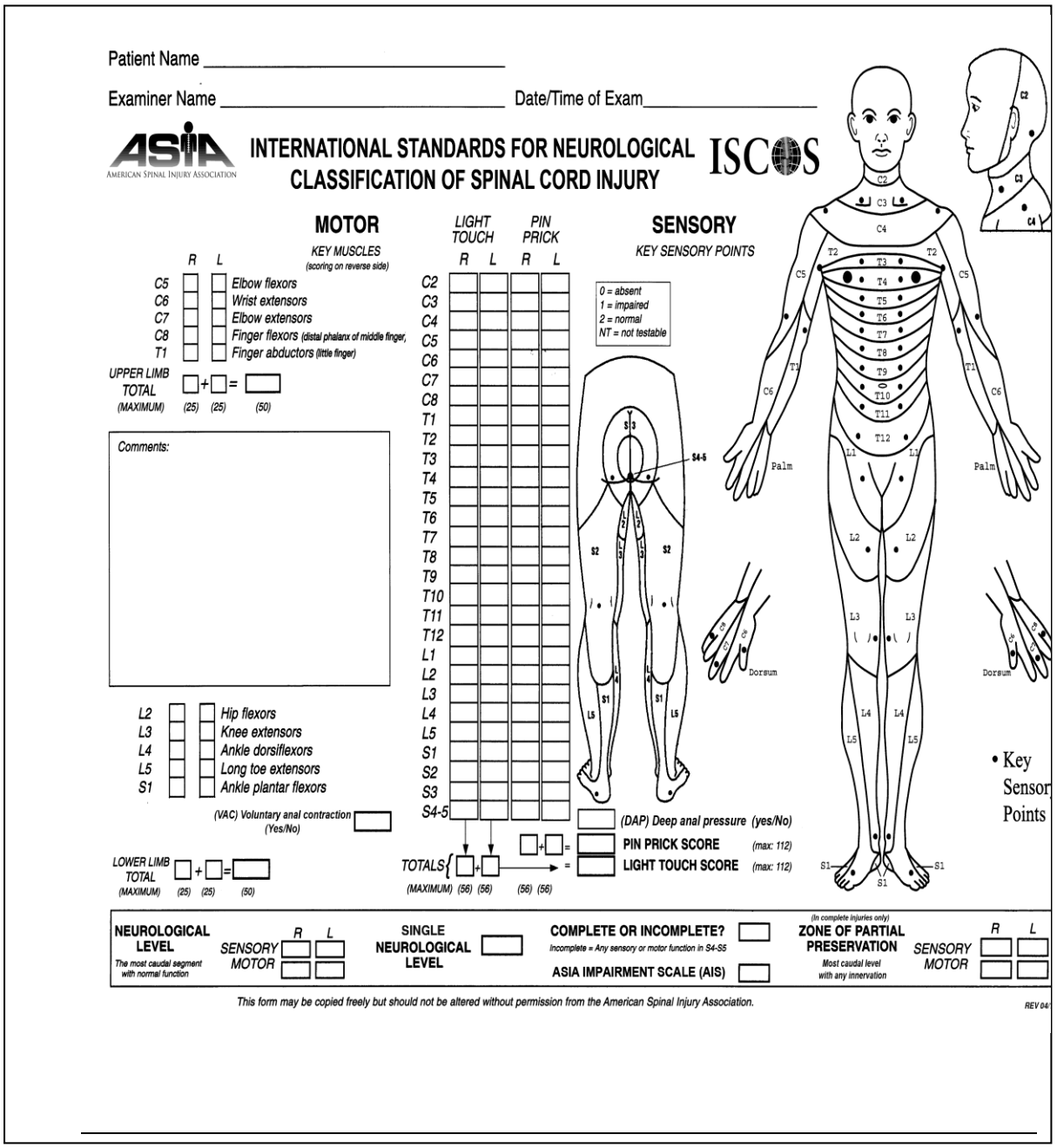
A sum of ₹ 33,000 (Rupees Thirty three thousand only) is sanctioned for 2 years.

Yours sincerely

Dr. Alfred Job Daniel
Principal& Chairperson (Research Committee)
Institutional Review Board

Chairperson (Research Committee) &
Principal
Christian Medical College
Vellore, Tamil Nadu, India

ANNEXURE IV



Patient Name _____

Examiner Name _____ Date/Time of Exam_____

ASIA American Spinal Injury Association

INTERNATIONAL STANDARDS FOR NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY

ISCOS

MOTOR

KEY MUSCLES (scoring on reverse side)

	R	L	
C5	☐	☐	Elbow flexors
C6	☐	☐	Wrist extensors
C7	☐	☐	Elbow extensors
C8	☐	☐	Finger flexors (distal phalanx of middle finger,
T1	☐	☐	Finger abductors (little finger)

UPPER LIMB TOTAL (MAXIMUM) ☐ + ☐ = ☐ (25) (25) (50)

Comments:

	R	L	
L2	☐	☐	Hip flexors
L3	☐	☐	Knee extensors
L4	☐	☐	Ankle dorsiflexors
L5	☐	☐	Long toe extensors
S1	☐	☐	Ankle plantar flexors

(VAC) Voluntary anal contraction (Yes/No) ☐

LOWER LIMB TOTAL (MAXIMUM) ☐ + ☐ = ☐ (25) (25) (50)

	LIGHT TOUCH R	LIGHT TOUCH L	PIN PRICK R	PIN PRICK L
C2				
C3				
C4				
C5				
C6				
C7				
C8				
T1				
T2				
T3				
T4				
T5				
T6				
T7				
T8				
T9				
T10				
T11				
T12				
L1				
L2				
L3				
L4				
L5				
S1				
S2				
S3				
S4-5				

TOTALS { ☐ + ☐ = ☐ (MAXIMUM) (56) (56) (56) (56)

SENSORY

KEY SENSORY POINTS

0 = absent
1 = impaired
2 = normal
NT = not testable

☐ (DAP) Deep anal pressure (yes/No)

☐ PIN PRICK SCORE (max: 112)

☐ LIGHT TOUCH SCORE (max: 112)

• Key Sensory Points

NEUROLOGICAL LEVEL
The most caudal segment with normal function
SENSORY R ☐ L ☐
MOTOR R ☐ L ☐

SINGLE NEUROLOGICAL LEVEL ☐

COMPLETE OR INCOMPLETE? ☐
Incomplete = Any sensory or motor function in S4-S5

ASIA IMPAIRMENT SCALE (AIS) ☐

(In complete injuries only)
ZONE OF PARTIAL PRESERVATION
Most caudal level with any innervation
SENSORY R ☐ L ☐
MOTOR R ☐ L ☐

REV 04/

Muscle Function Grading

0 = total paralysis

1 = palpable or visible contraction

2 = active movement, full range of motion (ROM) with gravity eliminated

3 = active movement, full ROM against gravity

4 = active movement, full ROM against gravity and moderate resistance in a muscle specific position.

5 = (normal) active movement, full ROM against gravity and full resistance in a muscle specific position expected from an otherwise unimpaired peson.

5* = (normal) active movement, full ROM against gravity and sufficient resistance to be considered normal if identified inhibiting factors (i.e. pain, disuse) were not present.

NT = not testable (i.e. due to immobilization, severe pain such that the patient cannot be graded, amputation of limb, or contracture of >50% of the range of motion).

ASIA Impairment (AIS) Scale

☐ **A = Complete.** No sensory or motor function is preserved in the sacral segments S4-S5.

☐ **B = Sensory Incomplete.** Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5 (light touch, pin prick at S4-S5: or deep anal pressure (DAP)), AND no motor function is preserved more than three levels below the motor level on either side of the body.

☐ **C = Motor Incomplete.** Motor function is preserved below the neurological level**, and more than half of key muscle functions below the single neurological level of injury (NLI) have a muscle grade less than 3 (Grades 0-2).

☐ **D = Motor Incomplete.** Motor function is preserved below the neurological level**, and at least half (half or more) of key muscle functions below the NLI have a muscle grade ≥ 3.

☐ **E = Normal.** If sensation and motor function as tested with the ISNCSCI are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. Someone without an initial SCI does not receive an AIS grade.

**For an individual to receive a grade of C or D, i.e. motor incomplete status, they must have either (1) voluntary anal sphincter contraction or (2) sacral sensory sparing with sparing of motor function more than three levels below the motor level for that side of the body. The Standards at this time allows even non-key muscle function more than 3 levels below the motor level to be used in determining motor incomplete status (AIS B versus C).

NOTE: When assessing the extent of motor sparing below the level for distinguishing between AIS B and C, the ***motor level*** on each side is used; whereas to differentiate between AIS C and D (based on proportion of key muscle functions with strength grade 3 or greater) the ***single neurological level*** is used.

Steps in Classification

The following order is recommended in determining the classification of individuals with SCI.

1. Determine sensory levels for right and left sides.
2. Determine motor levels for right and left sides.
   Note: in regions where there is no myotome to test, the motor level is presumed to be the same as the sensory level, if testable motor function above that level is also normal.
3. Determine the single neurological level.
   This is the lowest segment where motor and sensory function is normal on both sides, and is the most cephalad of the sensory and motor levels determined in steps 1 and 2.
4. Determine whether the injury is Complete or Incomplete. (i.e. absence or presence of sacral sparing)
   If voluntary anal contraction = **No** *AND all S4-5 sensory scores =* **0** *AND deep anal pressure =* **No,** *then injury is COMPLETE. Otherwise, injury is incomplete.*
5. Determine ASIA Impairment Scale (AIS) Grade:

Is injury Complete? If **YES,** AIS=A and can record ZPP (lowest dermatome or myotome on each side with some preservation)

NO ↓

Is injury motor Incomplete? If **NO**, AIS=B (Yes=voluntary anal contraction OR motor function more than three levels below the motor level on a given side, if the patient has sensory incomplete classification)

YES ↓

Are at least half of the key muscles below the single neurological level graded 3 or better?

NO ↓ AIS=C

YES ↓ AIS=D

If sensation and motor function is normal in all segments, AIS=E

Note: AIS E is used in follow-up testing when an individual with a documented SCI has recovered normal function. If at initial testing no deficits are found, the individual is neurologically intact; the ASIA Impairment Scale does not apply.